Que retenir des grands congrès et de l'actualité cardiologique en 2017

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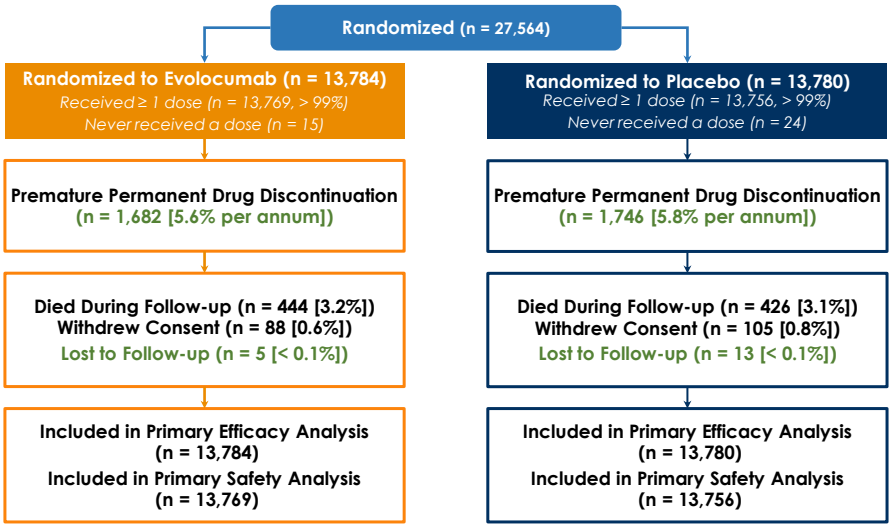
Evolocumab Outcomes Trial: Objective

FOURIER: **F**urther cardiovascular **OU**tcomes **R**esearch with PCSK9 **I**nhibition in subjects with **E**levated **R**isk

- Designed to test whether patients with established cardiovascular disease who are already on optimal cardiovascular therapy, including high to moderate intensity statins, benefit from maximal LDL-C reduction with evolocumab
- Additionally, will evaluate the clinical efficacy and safety of achieving unprecedented levels of low LDL-C with evolocumab
- Global randomized, placebo-controlled, double-blind trial (n = 27,564; 49 countries; 1,242 sites)

PCSK9, proprotein convertase subtilisin/kexin type 9.
Sabatine MS, *et al. Am Heart J.* 2016;173:94-101.
Sabatine MS, *et al . NEJM.* [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664

Disposition of Patients During the Study



Sabatine MS, et al. NEJM. [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664 (Supplemental Figure S1 – Trial Consort Diagram). Sabatine MS, et al. American College of Cardiology – 66th Annual Scientific Session Late-Breaking Clinical Trial. Washington, D.C. March 17, 2017.

Baseline Lipid-Lowering Therapies and Lipid Parameters

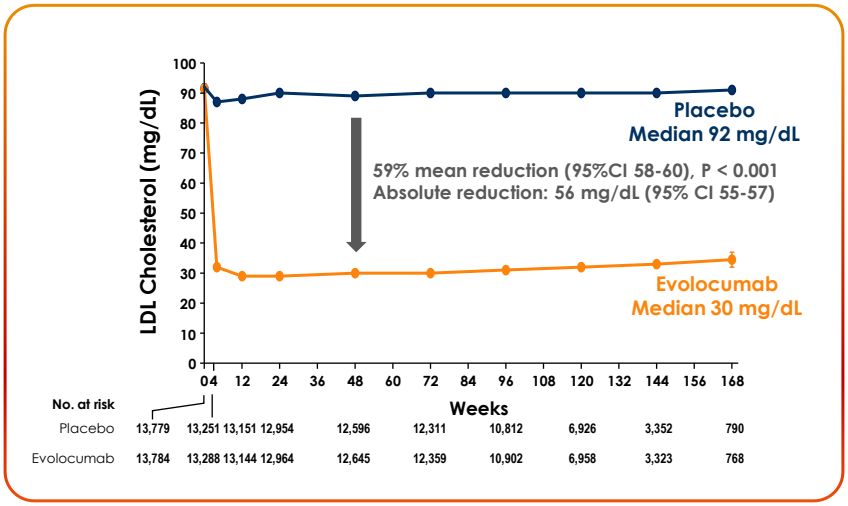
Characteristics	Evolocumab (N = 13,784)	Placebo (N = 13,780)
Statin use* – n (%)		
High intensity	9,585 (69.5)	9,518 (69.1)
Moderate intensity	4,161 (30.2)	4,231 (30.7)
Low intensity, unknown intensity, or no data	38 (0.3)	31 (0.2)
Ezetimibe – n (%)	726 (5.3)	714 (5.2)
Other cardiovascular medications – n/total n (%)		
Aspirin and/or $P2Y_{12}$ inhibitor	12,766/13,772 (92.7)	12,666/13,767 (92.0)
Beta-blocker	10,441/13,772 (75.8)	10,374/13,767 (75.4)
ACE inhibitor or ARB and/or aldosterone antagonist	10,803/13,772 (78.4)	10,730/13,767 (77.9)
Lipid measures - Median (IQR) – mg/dL		
LDL cholesterol – mg/dL	92 (80, 109)	92 (80, 109)
Total cholesterol – mg/dL	168 (151, 188)	168 (151, 189)
HDL cholesterol – mg/dL	44 (37, 53)	44 (37, 53)

*Statin intensity was categorized per the ACC/AHA Guidelines. Note, that in some countries where FOURIER was conducted, higher statin doses are not approved. HDL, high-density lipoprotein; LDL, low-density lipoprotein; Lp(a) = Lipoprotein(a); IQR = Inter-quartile range

Sabatine MS, *et al* . *NEJM*. [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664

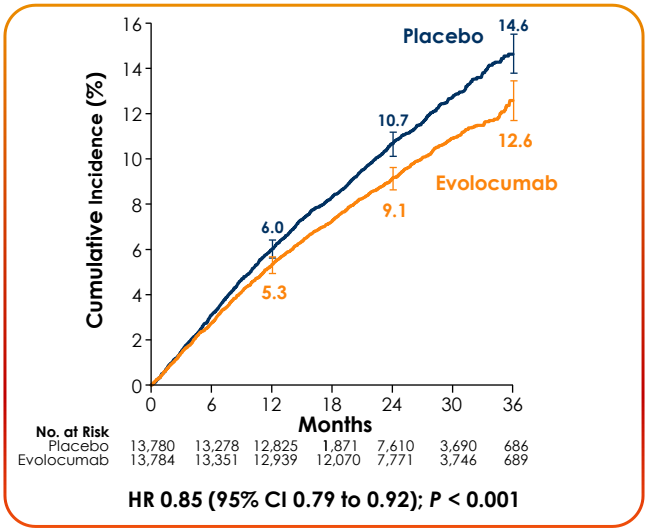
Malinowski HJ, *et all. J Clin Pharmacol.* 2008;48:900-908

Median LDL-C Levels Over Time: All Patients



Data shown are median values with 95% confidence intervals in the two arms; ITT.
Sabatine MS, *et al* . *NEJM*. [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664

Primary Endpoint: Composite of CV Death, MI, Stroke, Hospitalization for UA, or Coronary Revascularization



HR 0.85 (95% CI 0.79 to 0.92); *P* < 0.001

CV = Cardiovascular; MI = Myocardial infarction; UA = Unstable angina; HR = Hazard ratio
Sabatine MS, *et al* . *NEJM*. [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664

Primary, Key Secondary, and Other Endpoints

Outcome	Evolocumab (n = 13,784) n (%)	Placebo (n = 13,780) n (%)	HR (95% CI)	P-value‡
Primary endpoint*	1,344 (9.8)	1,563 (11.3)	0.85 (0.79-0.92)	<0.001
Key secondary endpoint†	816 (5.9)	1,013 (7.4)	0.80 (0.73-0.88)	<0.001
Other endpoints				
CV death	251 (1.8)	240 (1.7)	1.05 (0.88-1.25)	0.62
Death from any cause	444 (3.2)	426 (3.1)	1.04 (0.91-1.19)	0.54
MI	468 (3.4)	639 (4.6)	0.73 (0.65-0.82)	<0.001
Hospitalization for UA	236 (1.7)	239 (1.7)	0.99 (0.82-1.18)	0.89
Stroke	207 (1.5)	262 (1.9)	0.79 (0.66-0.95)	0.01
Coronary revascularization	759 (5.5)	965 (7.0)	0.78 (0.71-0.86)	<0.001
CV Death or Hospitalization for Worsening Heart Failure	402 (2.9)	408 (3.0)	0.98 (0.86-1.13)	0.82
Ischemic stroke or TIA	229 (1.7)	295 (2.1)	0.77 (0.65-0.92)	0.003
CTTC composite endpoint**	1,271 (9.2)	1,512 (11.0)	0.83 (0.77-0.90)	<0.001

*Time to CV death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization, whichever occurs first †CV death, myocardial infarction, or stroke, whichever occurs first ‡Given the hierarchical nature of the statistical testing, the P values for the primary and key secondary endpoint should be considered statistically significant, whereas all other P values should be considered nominal.
**CTTC stands for Cholesterol Treatment Trialists Collaboration and the composite endpoint consists of coronary heart death, nonfatal MI, stroke, or coronary revascularization
MI = Myocardial infarction; UA = Unstable angina; TIA = Transient ischemic attack
Sabatine MS, et al . NEJM. [published online ahead of print March 17, 2017]. doi: 10.1056/NEJMoa1615664

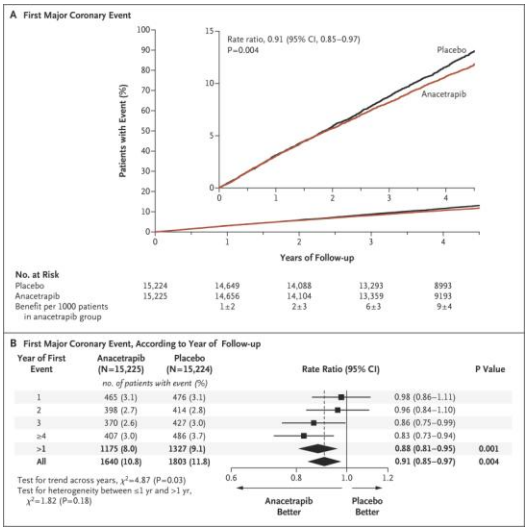
Effects of Anacetrapib on Blood Lipids and Lipoproteins at Trial Midpoint.

Table 2. Effects of Anacetrapib on Blood Lipids and Lipoproteins at Trial Midpoint.*

Lipid or Lipoprotein	Anacetrapib (N=15,225)	Placebo (N=15,224)	Absolute Difference†	Relative Difference
				percent
Mean LDL cholesterol (mg/dl)				
Direct method	38	64	−26	−41
Beta quantification‡	53	63	−11	−17
Mean non-HDL cholesterol (mg/dl)	79	96	−17	−18
Mean HDL cholesterol (mg/dl)	85	42	43	104
Mean apolipoprotein A1 (mg/dl)	160	118	42	36
Mean apolipoprotein B (mg/dl)	54	66	−12	−18
Mean triglycerides (mg/dl)	136	146	−10	−7
Mean lipoprotein(a) (nmol/liter)	43	58	−15	−25

The HPS3/TIMI55–REVEAL Collaborative Group. N Engl J Med 2017;377:1217-1227

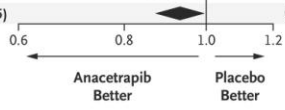
Essai First Major Coronary Event during Follow-up.



The HPS3/TIMI55–REVEAL Collaborative Group. N Engl J Med 2017;377:1217-1227

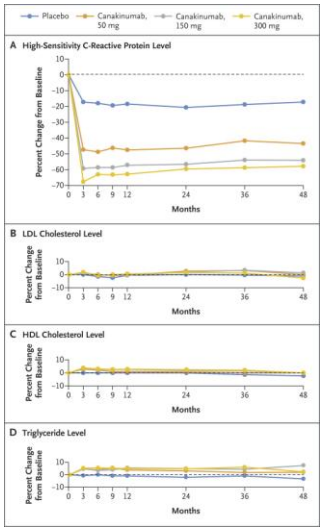
Primary and Secondary Outcomes.

Type of Event	Anacetrapib (N=15,225)	Placebo (N=15,224)	Rate Ratio (95% CI)	P Value
	no. of patients with event (%)			
Coronary death	388 (2.5)	420 (2.8)	0.92 (0.80–1.06)	0.25
MI	669 (4.4)	769 (5.1)	0.87 (0.78–0.96)	0.007
Coronary death or MI	**934 (6.1)**	**1048 (6.9)**	**0.89 (0.81–0.97)**	**0.008**
Coronary revascularization	1081 (7.1)	1201 (7.9)	0.90 (0.83–0.97)	0.01
Major coronary event	**1640 (10.8)**	**1803 (11.8)**	**0.91 (0.85–0.97)**	**0.004**
Presumed ischemic stroke	485 (3.2)	489 (3.2)	0.99 (0.87–1.12)	NA
Major atherosclerotic event	**1383 (9.1)**	**1483 (9.7)**	**0.93 (0.86–1.00)**	**0.052**
Major vascular event	**2068 (13.6)**	**2214 (14.5)**	**0.93 (0.88–0.99)**	**0.02**



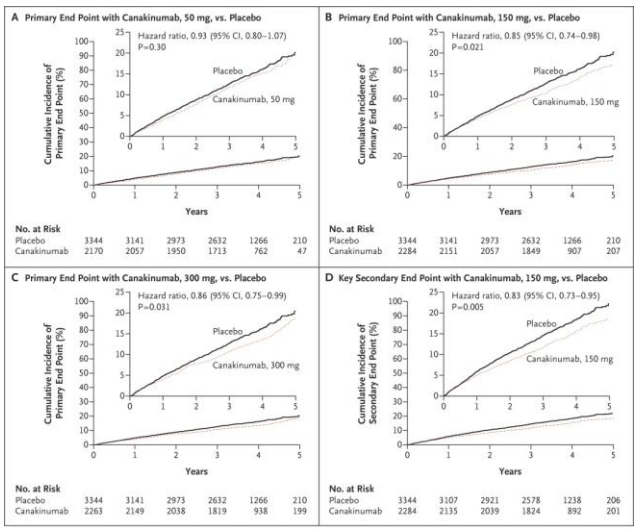
The HPS3/TIMI55–REVEAL Collaborative Group. N Engl J Med 2017;377:1217-1227

Effects of Canakinumab, as Compared with Placebo, on Plasma Levels of High-Sensitivity C-Reactive Protein, Low-Density Lipoprotein (LDL) Cholesterol, High-Density Lipoprotein (HDL) Cholesterol, and Triglycerides.



Ridker PM et al. N Engl J Med 2017;377:1119-1131

Cumulative Incidence of the Primary End Point and the Key Secondary Cardiovascular End Point.



Ridker PM et al. N Engl J Med 2017;377:1119-1131

SPYRAL HTN Clinical Program

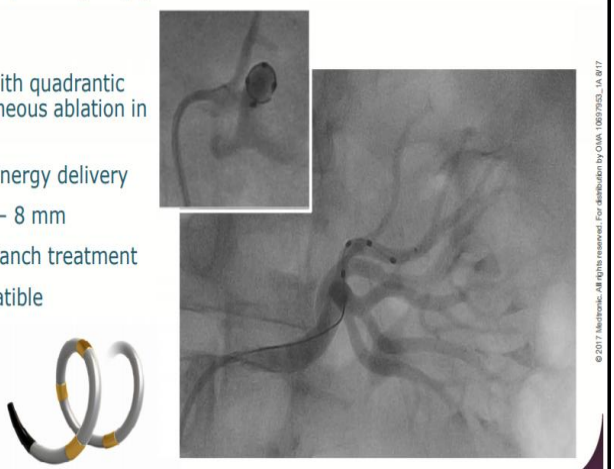
Addressing Confounding Factors[1] Identified from SYMPLICITY HTN-3

	Medications	Patients	Procedure
SYMPLICITY HTN-3	Drug changes and variable patient adherence	Heterogenous study population	Procedural experience and variability
SPYRAL HTN	Off and On Med studies with drug compliance testing	Excluding isolated systolic hypertension patients	Symplicity Spyral™ catheter, branch treatment, case proctoring

SPYRAL HTN Clinical Program

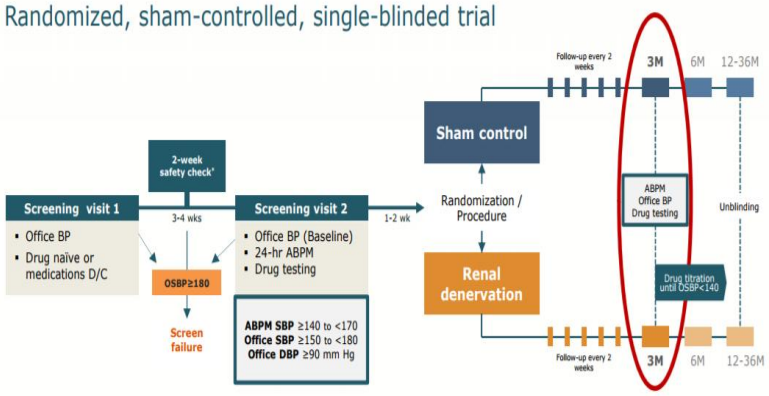
Study Device: Symplicity Spyral™ Catheter

- Multi-electrode catheter with quadrantic vessel contact for simultaneous ablation in up to 4 electrodes
- 60-second simultaneous energy delivery
- Vessel diameter range: 3 – 8 mm
- Flexible catheter allows branch treatment
- 6F guiding catheter compatible



SPYRAL HTN – OFF MED
Study Design

Randomized, sham-controlled, single-blinded trial



*Only for patients discontinuing anti-hypertensive medications

Kandzari D, et al. *Am Heart J.* 2016;171:82-91.

SPYRAL HTN – OFF MED
Patient Baseline Characteristics

Mean ± SD or % (N)	RDN (N = 38)	Sham Control (N = 42)
Age (years)	55.8 ± 10.1	52.8 ± 11.5
Male	68.4% (26/38)	73.8% (31/42)
BMI (kg/m^2)	29.8 ± 5.1	30.2 ± 5.1
Body weight (kg)	88.8 ± 16.6	90.9 ± 19.1
Diabetes (type 2)	2.6% (1/38)	7.1% (3/42)
Current smoker	10.5% (4/38)	23.8% (10/42)
Obstructive sleep apnea	7.9% (3/38)	7.1% (3/42)
Peripheral artery disease	2.6% (1/38)	0% (0/42)
Coronary artery disease†	0% (0/38)	4.8% (2/42)
Stroke and transient ischemic attack†	2.6% (1/38)	0% (0/42)
Myocardial infarction / acute coronary syndrome†	0% (0/38)	2.4% (1/42)

†These events occurred >3 months before randomization.

P = NS for differences in all baseline characteristics.

SPYRAL HTN – OFF MED
Baseline Blood Pressure

Mean ± SD	RDN	Sham Control
Office measurements	N = 38	N = 42
Office SBP (mm Hg)	162.0 ± 7.6	161.4 ± 6.4
Office DBP (mm Hg)	99.9 ± 6.8	101.5 ± 7.5
Office heart rate (bpm)	71.1 ± 11.0	73.4 ± 9.8
24-hour measurements	N = 37	N = 42
Mean 24-hour SBP (mm Hg)	153.4 ± 9.0	151.6 ± 7.4
Mean 24-hour DBP (mm Hg)	99.1 ± 7.7	98.7 ± 8.2
Mean 24-hour heart rate (bpm)	72.3 ± 10.9	75.5 ± 11.5

P = NS for differences in all baseline characteristics.

SPYRAL HTN – OFF MED
Procedural Details

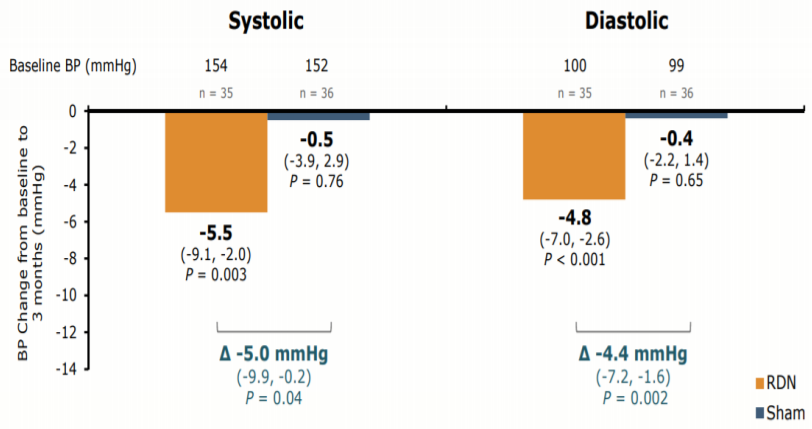
Mean ± SD	RDN (N = 38)	Sham Control (N = 42)
Number of main renal arteries treated per patient	2.2 ± 0.5	NA
Number of branches treated per patient	5.2 ± 2.5	NA
Total number of ablations per patient	43.8 ± 13.1	NA
Main artery ablations	17.9 ± 10.5	NA
Branch ablations	25.9 ± 12.8	NA
Treatment time (min)	57.1 ± 19.7	NA
Contrast volume used (cc)	251.0 ± 99.4	83.3 ± 38.5

SPYRAL HTN – OFF MED
Medication Adherence

% (n)	RDN	Sham Control	*P*
No anti-HTN drug identified by drug testing:			
At baseline	92.1% (35/38)	88.1% (37/42)	0.72
At 3 months	94.3% (33/35)	92.7% (38/41)	1.00
At baseline and 3 months	88.6% (31/35)	82.9% (34/41)	0.53
Patients meeting escape criteria (n)	2	4	

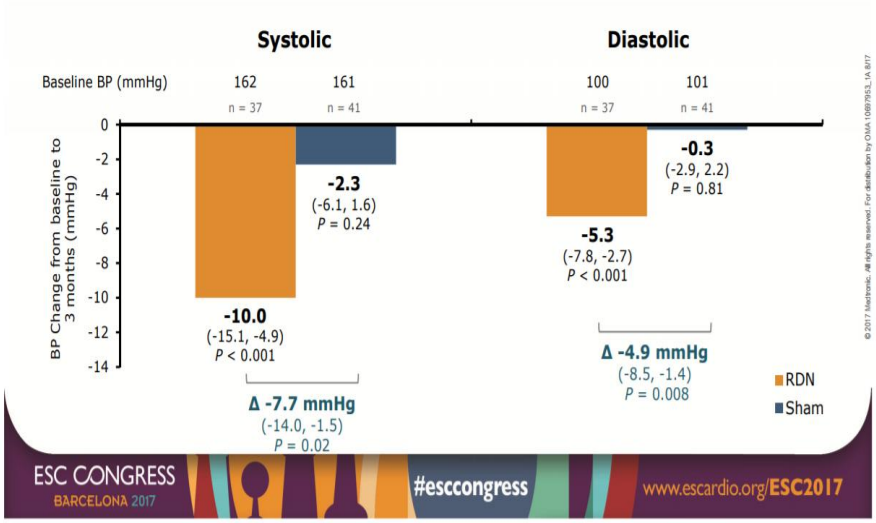
Drug testing of Urine and Serum by tandem HPLC and Mass Spectroscopy.

SPYRAL HTN – OFF MED
Blood Pressure Change from Baseline to 3 Months: 24-Hr ABPM



SPYRAL HTN – OFF MED

Blood Pressure Change from Baseline to 3 Months: Office BP

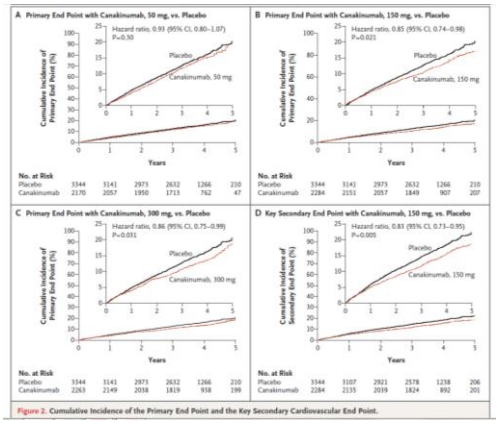


SPYRAL HTN Clinical Program

Advances of SPYRAL HTN Compared to SYMPLICITY HTN-3

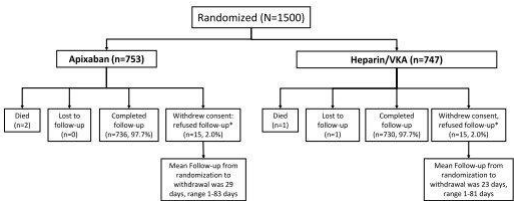
	Medications	Patients	Procedure
SYMPLICITY HTN-3	▪ 5.1 prescribed anti-HTN drugs at randomization ▪ No drug adherence testing	▪ Resistant hypertension patients (OSBP 180 ± 16) ▪ No diastolic cutoff	▪ Mono-electrode, sequential ablation system ▪ Mostly inexperienced operators without proctoring ▪ Main artery RDN only ▪ Ablations per pt: 11.2 ± 2.8
SPYRAL HTN OFF MED	▪ No anti-HTN drugs at time of randomization ▪ Drug adherence testing by serum and urine	▪ Moderate hypertension patients (OSBP 162 ± 7) ▪ Excluding ISH patients (ODBP 101 ± 7)	▪ Four-electrode, simultaneous ablation system ▪ Highly experienced operators with proctoring ▪ Main + branches RDN ▪ Ablations/pt: 43.8 ± 13.1

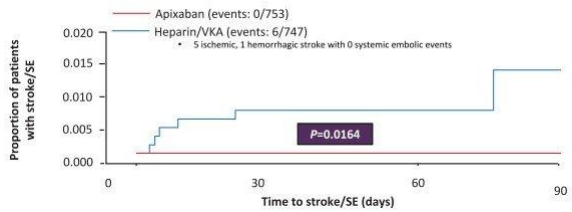
CANTOS: inflammation et atheroclerose



Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease. N Engl J Med 2017;NEJMoa1707914.

Apixaban et Cardioversion: etude EMANATE





DETOX2-AMI

Objectif

L'objectif était d'évaluer l'effet de l'oxygénothérapie sur la mortalité à 1 an chez les patients suspects d'infarctus du myocardique normoxémique.

Design de l'étude

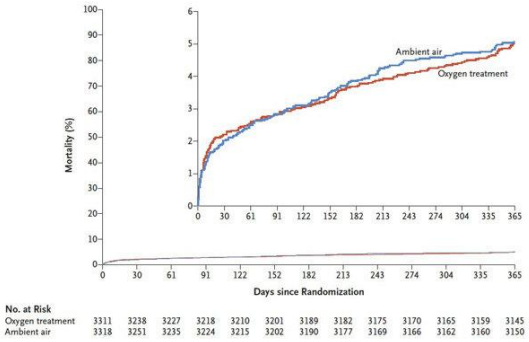
Ils étaient randomisés pour recevoir une oxygénothérapie au masque à 6 litres par minute pendant 6 à 12 heures ou étaient ventilés en air ambiant sans masque.

Le critère de jugement principal était la mortalité à 1 an.

Les critères de jugement secondaires étaient la mortalité à 1 mois, une ré hospitalisation pour insuffisance cardiaque et la mortalité cardio-vasculaire.

Résultats

Dans ce travail, 6 629 patients ont été inclus, 3 311 dans le groupe oxygénothérapie et 3 318 dans le groupe air ambiant. L'âge médian était de 68 ans et 2/3 des patients étaient de sexe masculin. Au total, 2952 infarctus du myocarde avec sus-décalage du segment ST ont été inclus. Les caractéristiques à l'admission étaient comparables entre les 2 groupes. La durée de l'oxygénothérapie était de 11,6 heures.

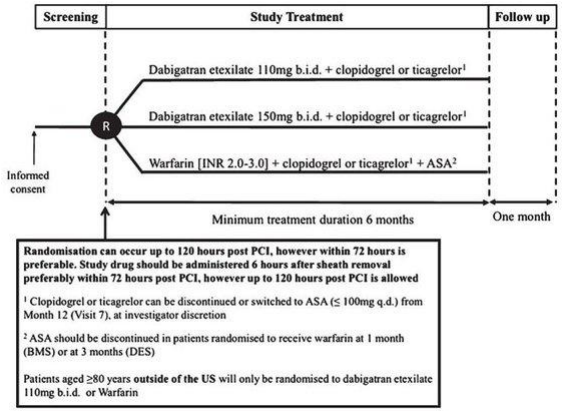


No. at Risk

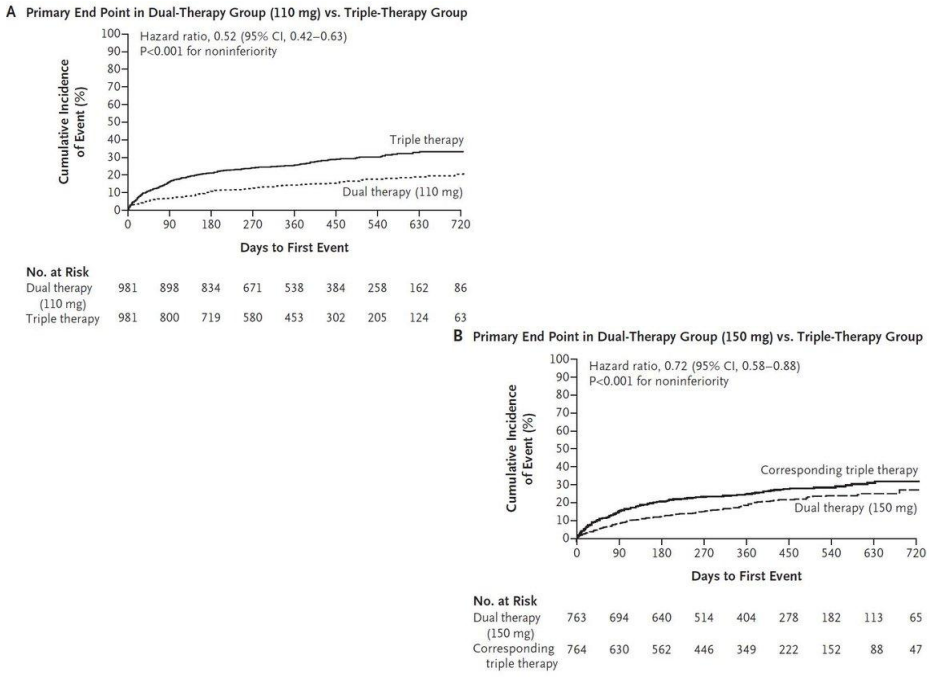
Oxygen treatment	3311	3238	3227	3218	3210	3201	3189	3182	3175	3170	3165	3159	3145
Ambient air	3318	3251	3235	3224	3215	3202	3190	3177	3169	3166	3162	3160	3150

Hofmann R, James SK, Jernberg T, Lindahl B, Erlinge D, Witt N, et al.
Oxygen Therapy in Suspected Acute Myocardial Infarction. N Engl J Med. 2017 Aug 28;

Dabigatran post PCI : REDUAL PCI

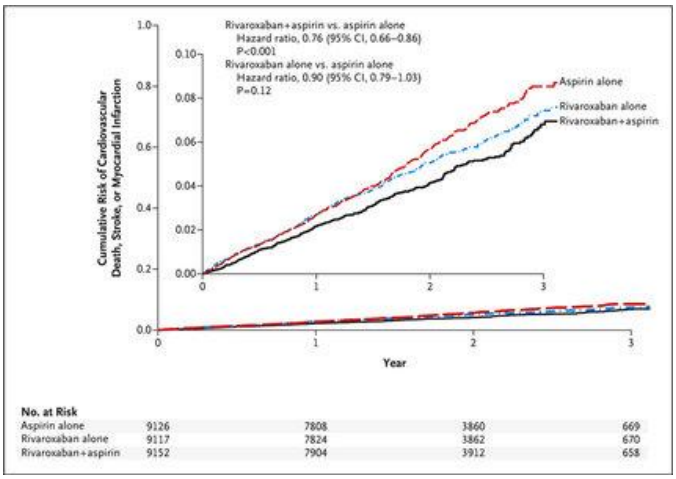


Cannon CP et al. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. N Engl J Med. 2017 Aug 27. -



Cannon CP et al. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. N Engl J Med. 2017 Aug 27. -

Rivaroxaban: étude COMPASS



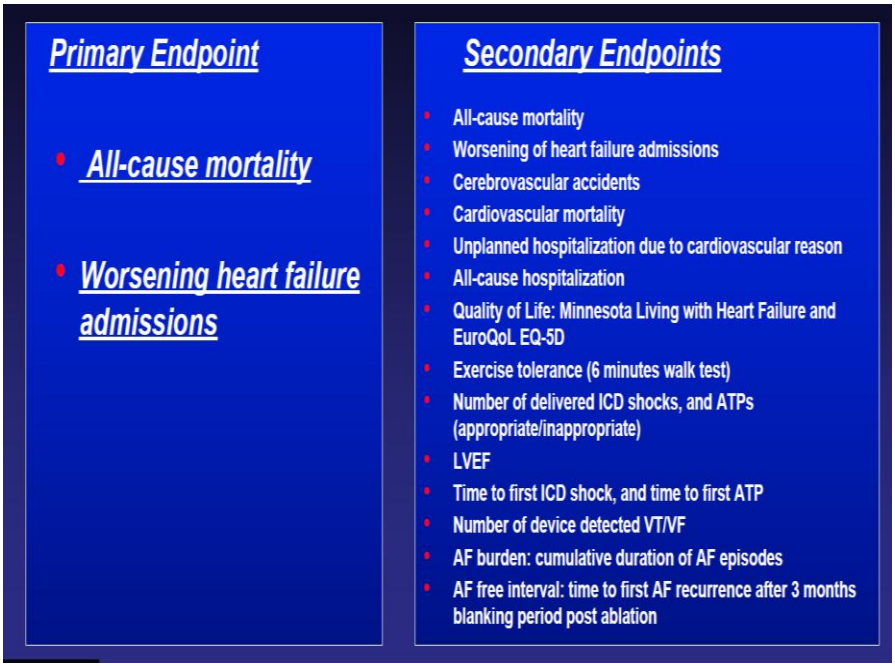
Eikelboom et al. Rivaroxaban with or without aspirine in stable cardiovascular disease. NEJM august 2017

Objectif

Ablation versus traitement conventionnel chez des IC avec FA

sur la survenue de critères durs

(mortalité – progression de l'insuffisance cardiaque)

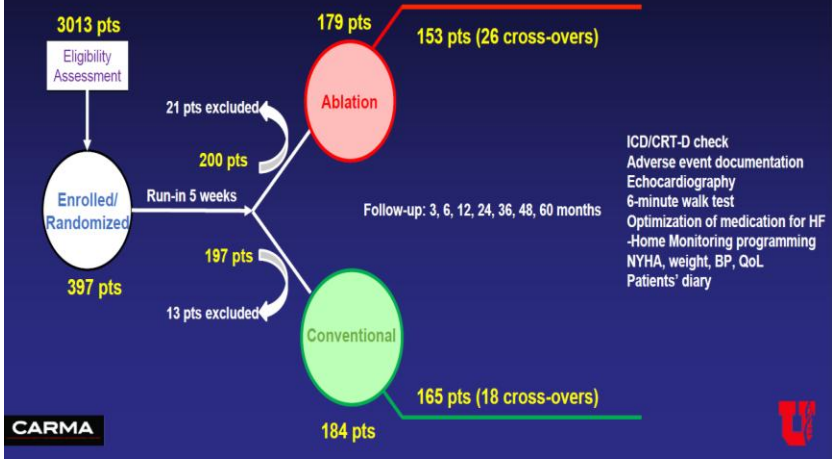


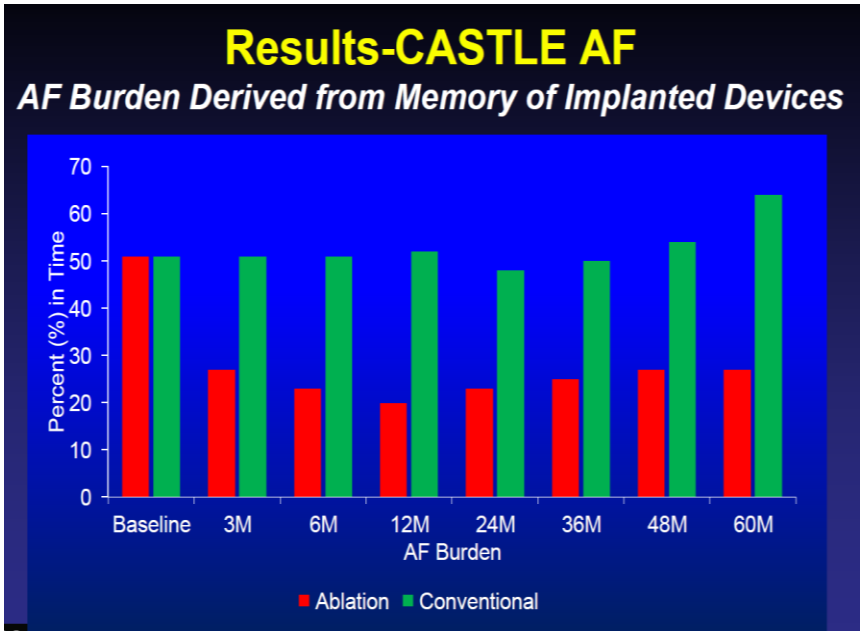
CASTLE-AF
Inclusion Criteria

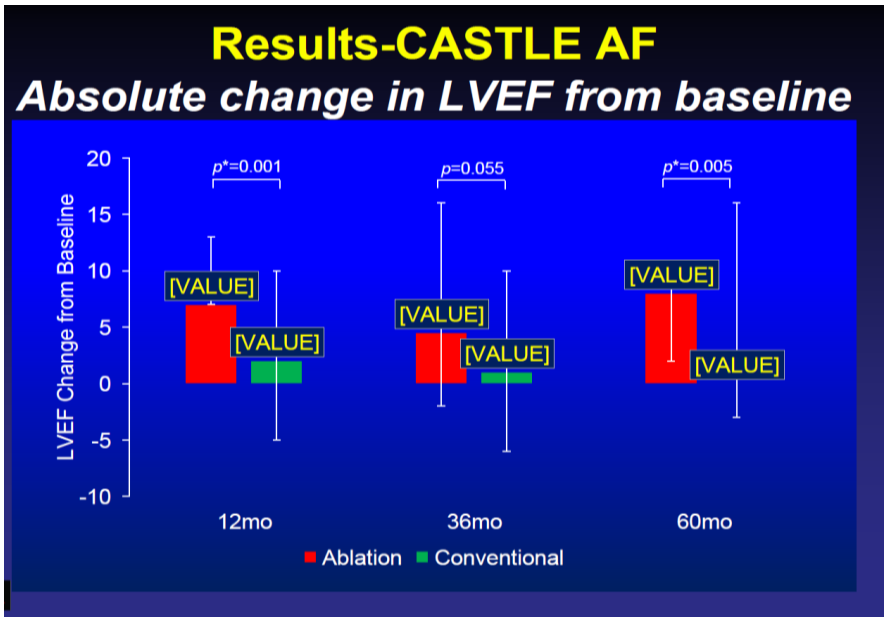
- Symptomatic paroxysmal or persistent AF
- Failure or intolerance to ≥ 1 or unwillingness to take AAD
- LVEF ≤ 35%
- NYHA class ≥ II
- ICD/CRT-D with Home Monitoring capabilities already implanted due to primary or secondary prevention

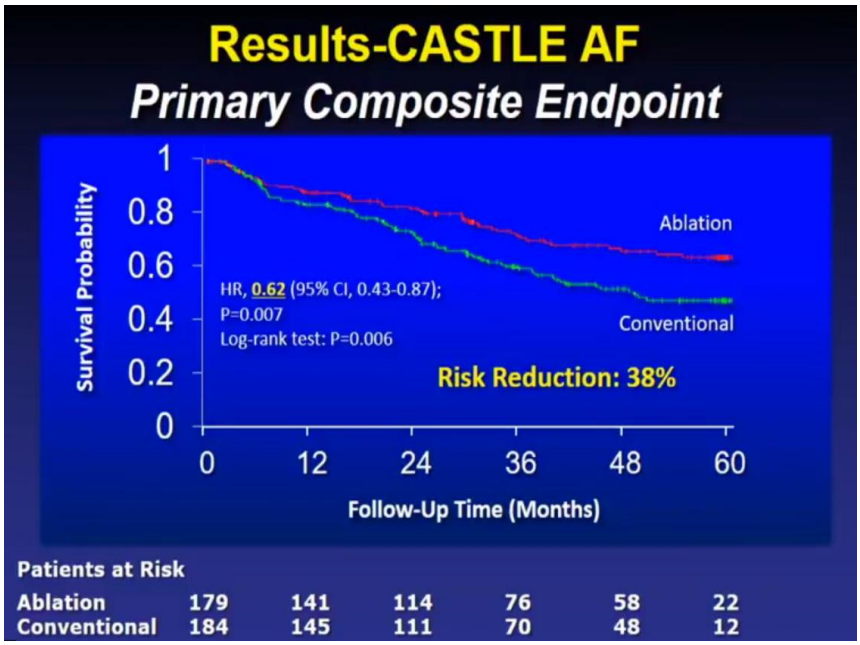
Study Design— CASTLE-AF

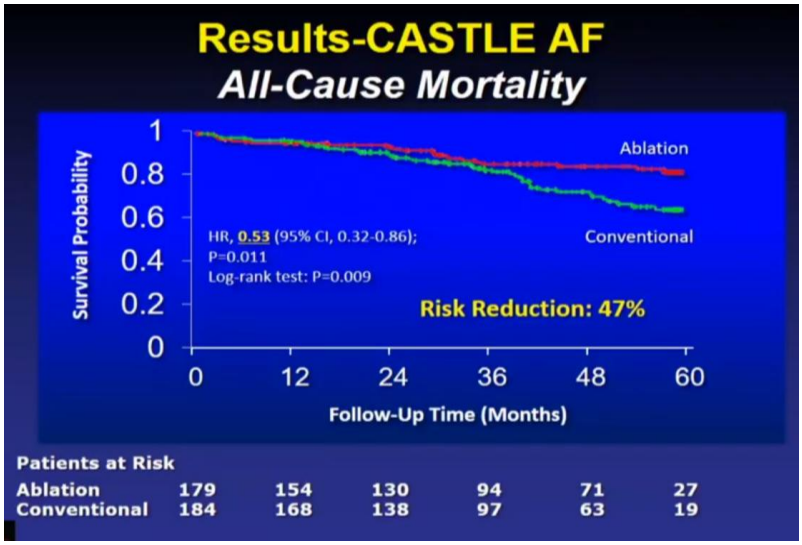
- Investigator initiated, Prospective, Multicenter (31 sites, 9 countries), Randomized, Controlled

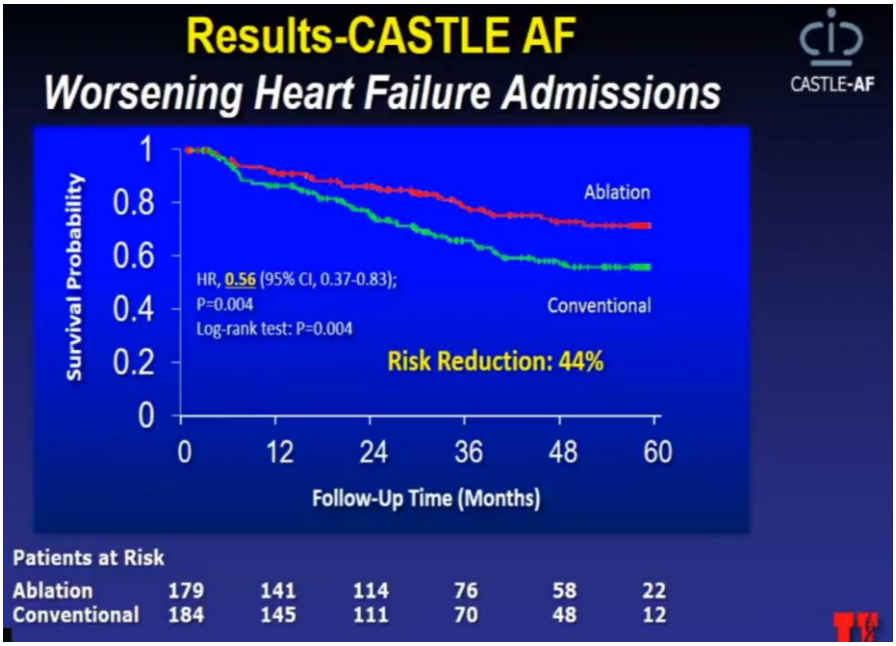


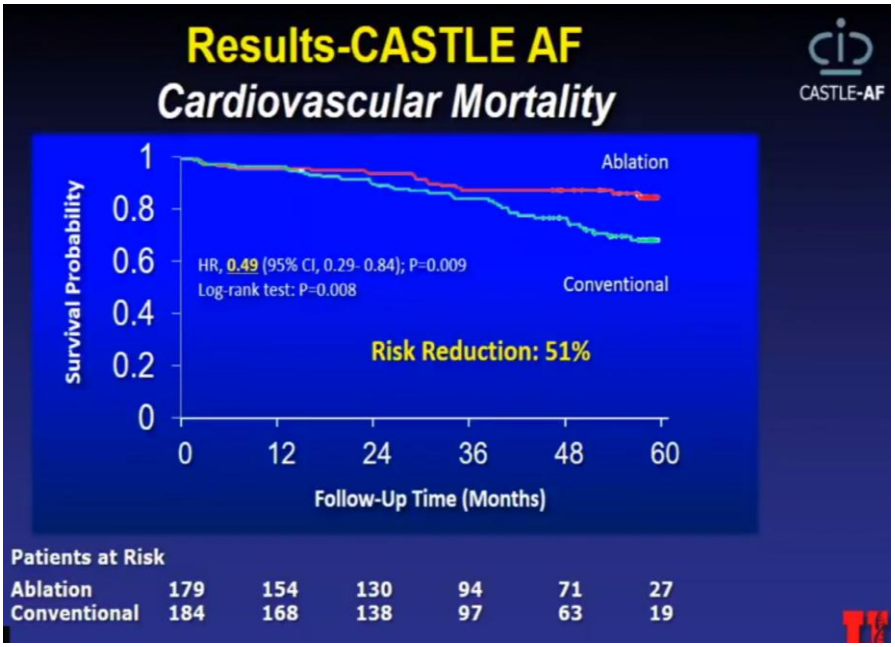

Results-CASTLE AF
AF Burden Derived from Memory of Implanted Devices
Percent (%) in Time
70
60
50
40
30
20
10
0
Baseline
3M
6M
12M
24M
36M
48M
60M
AF Burden
Ablation
Conventional


Results-CASTLE AF
Absolute change in LVEF from baseline
LVEF Change from Baseline
20
15
10
5
0
-5
-10
p*=0.001
p=0.055
p*=0.005
[VALUE]
[VALUE]
[VALUE]
[VALUE]
[VALUE]
[VALUE]
12mo
36mo
60mo
Ablation
Conventional


Results-CASTLE AF
Primary Composite Endpoint
Survival Probability
1
0.8
0.6
0.4
0.2
0
Ablation
HR, 0.62 (95% CI, 0.43-0.87);
P=0.007
Log-rank test: P=0.006
Conventional
Risk Reduction: 38%
0
12
24
36
48
60
Follow-Up Time (Months)
Patients at Risk
Ablation 179 141 114 76 58 22
Conventional 184 145 111 70 48 12


Results-CASTLE AF
All-Cause Mortality
Survival Probability
1
0.8
0.6
0.4
0.2
0
Ablation
HR, 0.53 (95% CI, 0.32-0.86);
P=0.011
Log-rank test: P=0.009
Conventional
Risk Reduction: 47%
0
12
24
36
48
60
Follow-Up Time (Months)
Patients at Risk
Ablation 179 154 130 94 71 27
Conventional 184 168 138 97 63 19


Results-CASTLE AF
Worsening Heart Failure Admissions
CASTLE-AF
Survival Probability
1
0.8
0.6
0.4
0.2
0
Ablation
HR, 0.56 (95% CI, 0.37-0.83);
P=0.004
Log-rank test: P=0.004
Conventional
Risk Reduction: 44%
0
12
24
36
48
60
Follow-Up Time (Months)
Patients at Risk
Ablation 179 141 114 76 58 22
Conventional 184 145 111 70 48 12


Results-CASTLE AF
Cardiovascular Mortality
CASTLE-AF
Survival Probability
1
0.8
0.6
0.4
0.2
0
Ablation
HR, 0.49 (95% CI, 0.29- 0.84); P=0.009
Log-rank test: P=0.008
Conventional
Risk Reduction: 51%
0
12
24
36
48
60
Follow-Up Time (Months)
Patients at Risk
Ablation 179 154 130 94 71 27
Conventional 184 168 138 97 63 19

Conclusion

- Réduire la Pression Arterielle avec la Denervation rénale
- Réduire les LDL avec les anti PCSK9
- Restaurer le HDL avec l'ancatrapib
- Reduire l'inflammation
- Reduire la FA par ablation chez l'insuffisant cardiaque
- Rivaroxaban et risque CV
- Refuser Dabigatran dans la prise en charge post PCI
- Reduire la FA avec apixaban