PCI: The Year in Review -- 2017

Neal S. Kleiman, MD

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DES vs BMS: NORSTENT Trial

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- 9,013 Patients randomized to DES vs BMS between 9/2008 and 2/2011 (20,663 total underwent PCI In Norway)
- Median follow-up 59 months
- Primary EP: death/spontaneous MI at 6 years
- DAPT x 9 months
- 82% Everolimus-eluting stents; 11.9% zotarolimus-eluting

Bonaa. NEJM.2016;375:1242

NORSTENT: DES vs BMS

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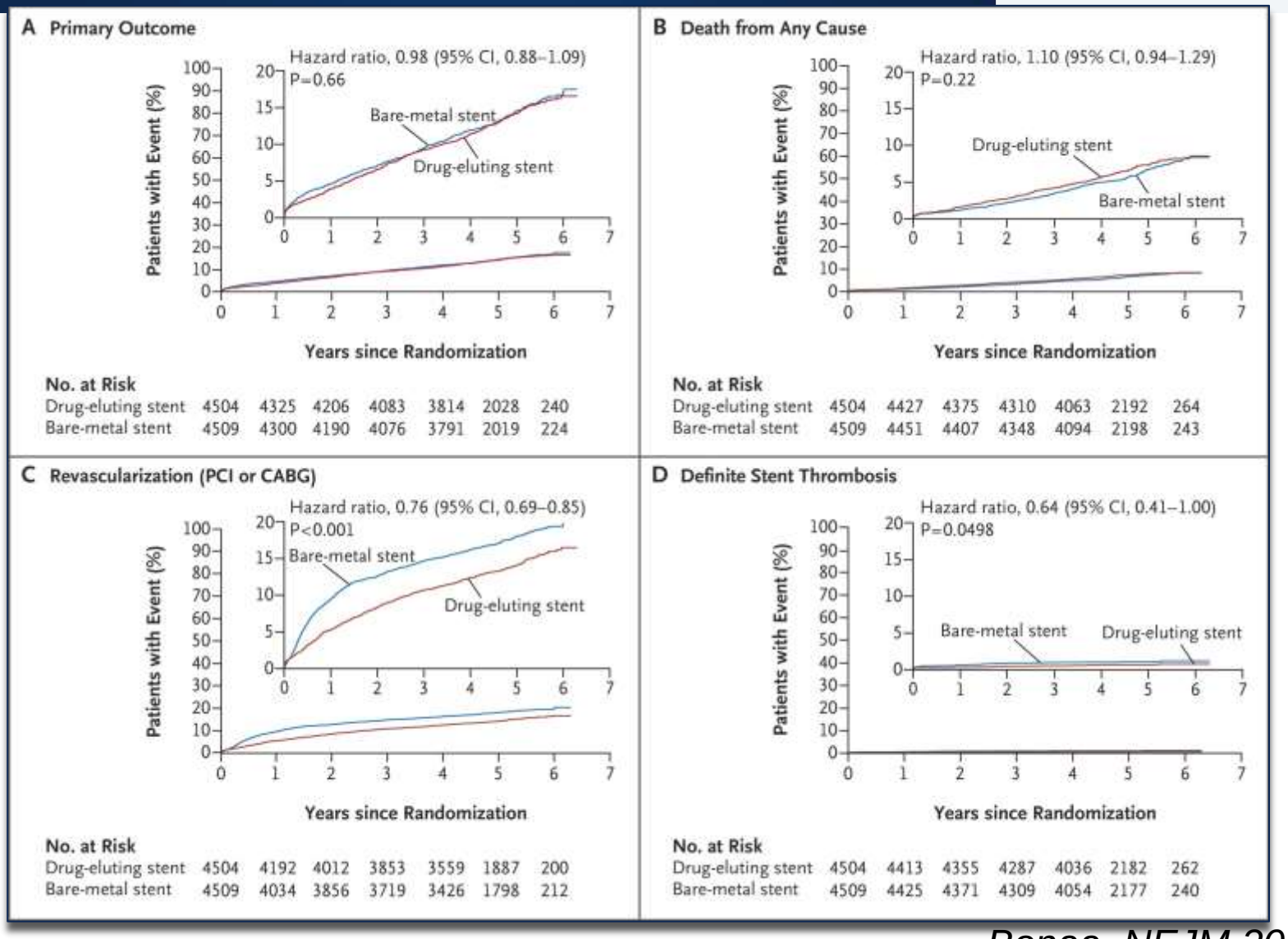

Bonaa. NEJM.2016;375:1242

Balancing the Evidence Base on Coronary Stents

Eric R. Bates, M.D.

The development of percutaneous coronary intervention (PCI) t… structive corona… invasive revascu… bypass grafting… cal outcomes a… catheters were l… early interventi… thrombotic th…

studies.

Of the 20,6… centers in Nc… 12,425 met the… (72.5%) were … contemporary… stents. After a … were no signif… the primary composite outcome of death from any cause or nonfatal spontaneous myocardial infarc-

risk of late stent thrombosis. Now in the fourth …al …i- …n- …ve …n- …s-

Drug-Eluting or Bare-Metal Stents for Coronary Artery Disease

TO THE EDITOR: The results from the Norwegian Coronary Stent Trial (NORSTENT) (Sept. 29 issue)[1] showing that mortality was not significantly lower with drug-eluting stents than with bare-metal stents are unsurprising, given that stents have not been shown to affect survival. Drug-eluting stents are highly effective in reducing recurrent symptoms that require revascularization, which is their designed intent. In the accompanying editorial, Bates[2] suggests that bare-metal stents are preferred over drug-eluting stents in patients who cannot adhere to dual-antiplatelet therapy owing to a high risk of bleeding, ostensibly because bare-metal stents are associated with a lower risk of stent thrombosis. However, in NORSTENT, the rate of stent thrombosis was 36% lower in the patients who received drug-eluting stents than in those who received bare-

in large-diameter vessels, in which the risk of restenosis is low; however, in the Basel Stent Kosten-Effektivitäts Trial–Prospective Validation Examination (BASKET-PROVE) trial, wherein only stents that were 3.0 mm or more in diameter were used, the rate of repeat revascularization was lower with drug-eluting stents than with bare-metal stents.[3] We believe there is little role remaining for bare-metal stents in the contemporary practice of interventional cardiology.

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with a large vessel diameter in whom restenosis rates are low,[7] those who cannot complete the lon-

Leaders Free Trial

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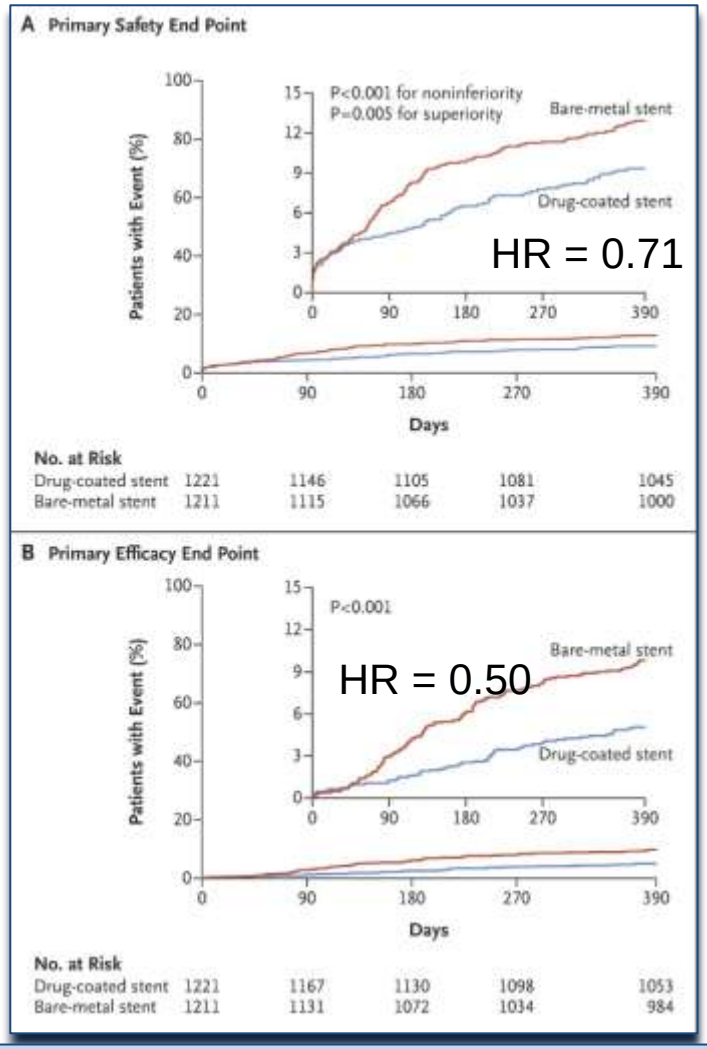
- 2,466 Patients at **high risk** for bleeding
- Polymer-free biolimus-eluting vs bare metal stent + one month of DAPT
- 36% were on oral anticoagulants
- Primary EPs
  - Safety: CV death, MI, definite or probable ST
  - Efficacy: TLR



TLR 5.1% vs 10.0% (P<0.001)
Stent Thrombosis: 1.9% vs 2.2% (P=0.56)

Urban. NEJM.2015;373:2038.

LEADERS FREE: 2 Year Follow-Up

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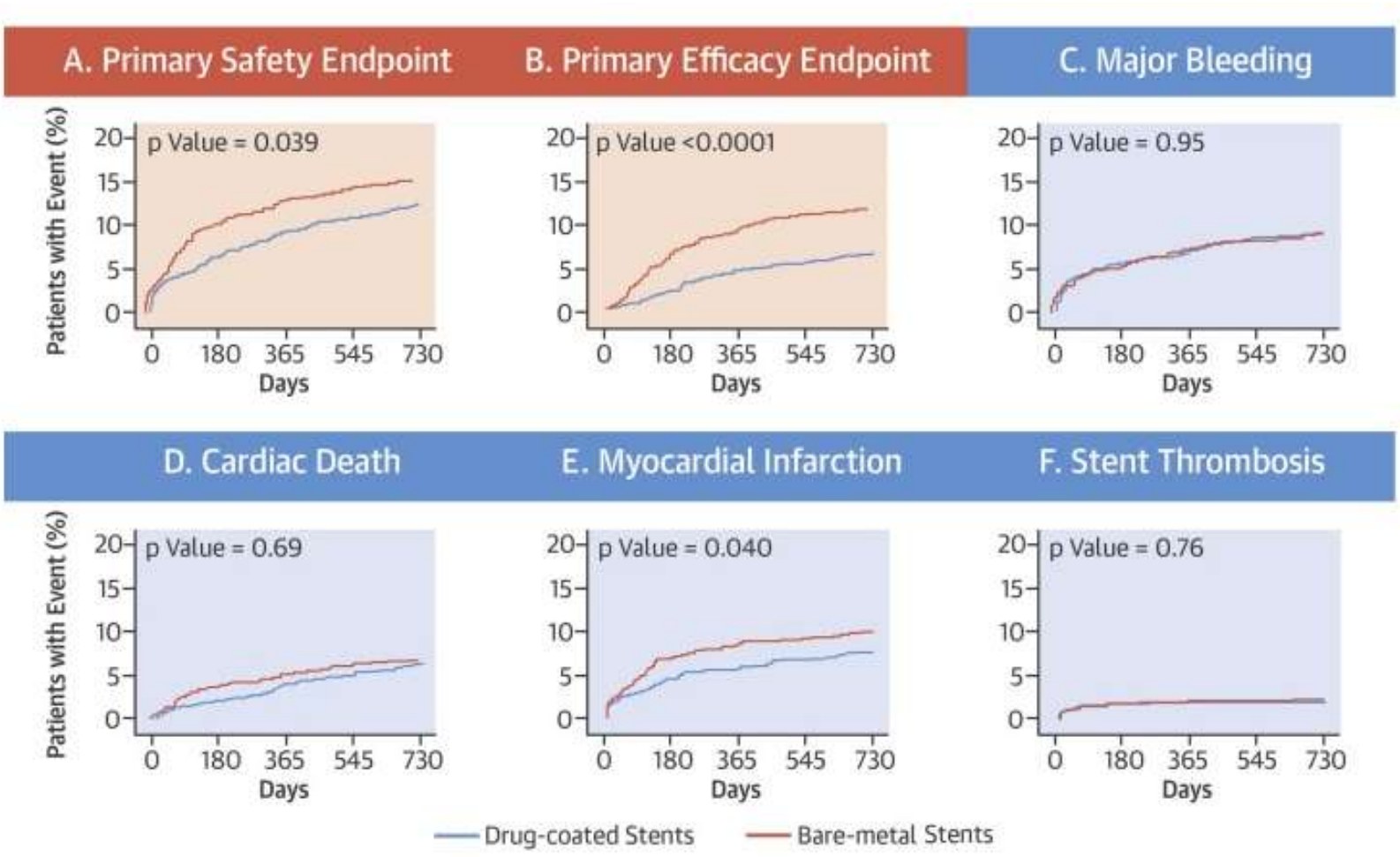

Garot, P. et al. J Am Coll Cardiol. 2017;69(2):162-71.

PRECOMBAT Trial: Five Year Follow-up

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BACKGROUND In a previous randomized trial, we found that percutaneous coronary intervention (PCI) was not inferior to coronary artery bypass grafting (CABG) for the treatment of unprotected left main coronary artery stenosis at 1 year.

OBJECTIVES This study sought to determine the 5-year outcomes of PCI compared with CABG for the treatment of unprotected left main coronary artery stenosis.

METHODS We randomly assigned 600 patients with unprotected left main coronary artery stenosis to undergo PCI with a sirolimus-eluting stent (n = 300) or CABG (n = 300). The primary endpoint was a major adverse cardiac or cerebrovascular event (MACCE: a composite of death from any cause, myocardial infarction, stroke, or ischemia-driven target vessel revascularization) and compared on an intention-to-treat basis.

RESULTS At 5 years, MACCE occurred in 52 patients in the PCI group and 42 patients in the CABG group (cumulative event rates of 17.5% and 14.3%, respectively; hazard ratio [HR]: 1.27; 95% confidence interval [CI]: 0.84 to 1.90; p = 0.26). The 2 groups did not differ significantly in terms of death from any cause, myocardial infarction, or stroke as well as their composite (8.4% and 9.6%; HR, 0.89; 95% CI, 0.52 to 1.52; p = 0.66). Ischemia-driven target vessel revascularization occurred more frequently in the PCI group than in the CABG group (11.4% and 5.5%, respectively; HR: 2.11; 95% CI: 1.16 to 3.84; p = 0.012).

CONCLUSIONS During 5 years of follow-up, our study did not show significant difference regarding the rate of MACCE between patients who underwent PCI with a sirolimus-eluting stent and those who underwent CABG. However, considering the limited power of our study, our results should be interpreted with caution. (Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease [PRECOMBAT]; NCT00422968) (J Am Coll Cardiol 2015;65:2198-206) © 2015 by the American College of Cardiology Foundation.

Study Design

2900 pts with unprotected left main disease

SYNTAX score ≤32

Consensus agreement of eligibility and equipoise by heart team

No (N=1000) → Enrollment registry

Yes (N=1900)

Stratified by diabetes, SYNTAX score and center → R

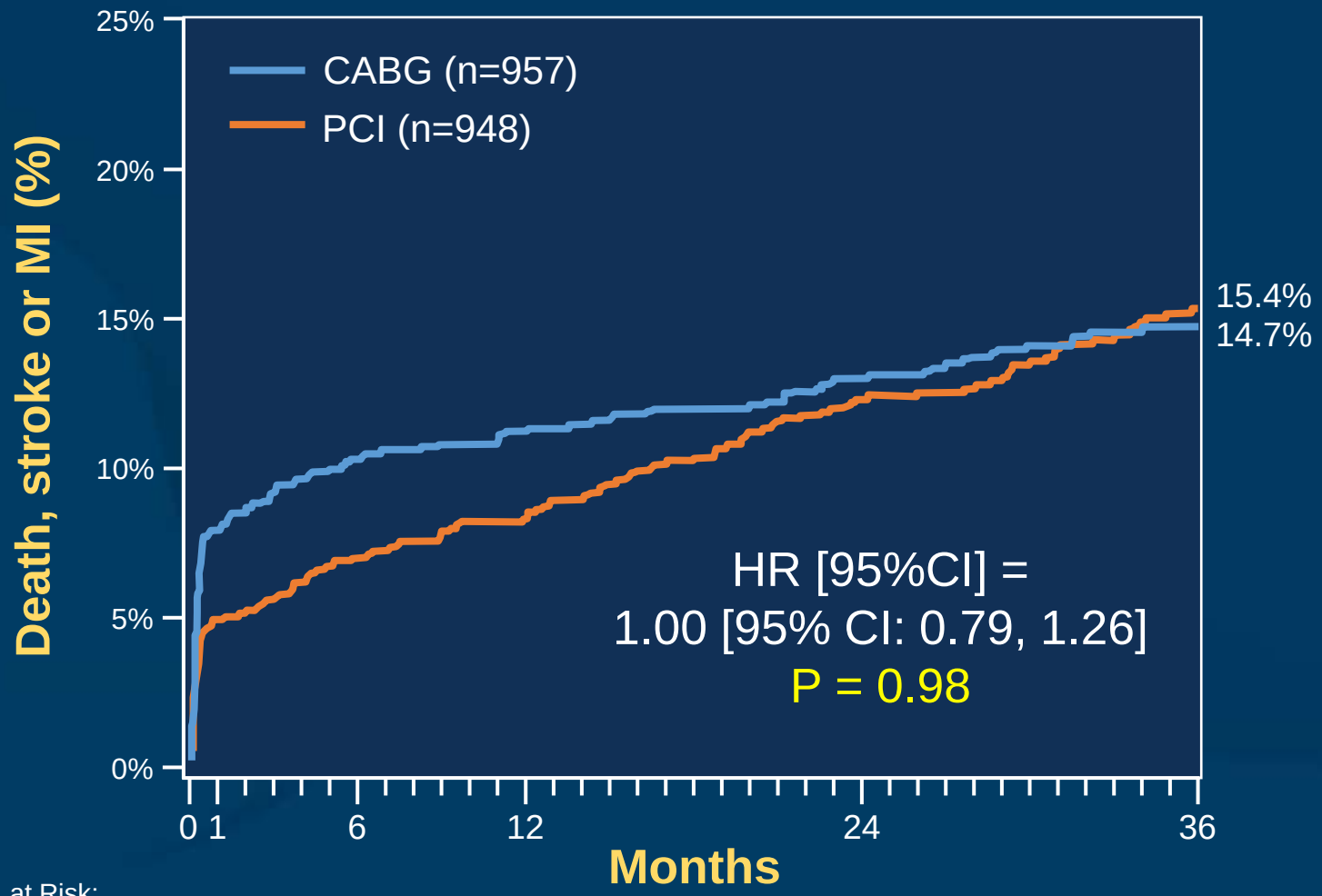
- PCI (Xience EES) (N=950)
- CABG (N=950)

Follow-up: 1 month, 6 months, 1 year, annually through 5 years

Primary endpoint: Measured at a median 3-yr FU, minimum 2-yr FU

Primary Endpoint

Death, Stroke or MI at 3 Years



No. at Risk:

PCI	948	896	875	850	784	445
CABG	957	868	836	817	763	458

Primary and Hierarchical Secondary Clinical Outcomes

	PCI (n=948)	CABG (n=957)	Diff [upper confidence limit]	P_{NI}	HR [95%CI]	P_{Sup}
Primary endpoint						
Death, stroke or MI at 3 years	15.4%	14.7%	0.7% [4.0%]†	0.018	-	-
Secondary endpoints						
Death, stroke or MI at 30 days	4.9%	7.9%	-3.1% [-1.2%]††	<0.001	-	-
Death, stroke, MI or ischemia-driven revasc at 3 years	23.1%	19.1%	4.0% [7.2%]††	0.01	-	-
Death, stroke or MI at 3 years	15.4%	14.7%	-	-	1.00 [0.79, 1.26]	0.98

The pre-specified non-inferiority margins (deltas) were 4.2% for death, stroke or MI at 3 years, 2.0% for death, stroke or MI at 30 days, and 8.4% for death, stroke, MI or ischemia-driven revascularization at 3 years.
†Upper 97.5% confidence limit; ††Upper 95.0% confidence limit.

Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis

Nordic–Baltic–British left main revascularisation study (NOBLE)
A prospective, randomised, open-label, non-inferiority trial

NOBLE

Evald Høj Christiansen

Timo Mäkikallio, Niels R Holm, Mitchell Lindsay, Mark S Spence, Andrejs Erglis, Ian B A Menown, Thor Trovik, Markku Eskola, Hannu Romppanen, Thomas Kellerth, Jan Ravkilde, Lisette O Jensen, Gintaras Kalinauskas, Rikard B A Linder, Markku Pentikainen, Anders Hervold, Adrian Banning, Azfar Zaman, Jamen Cotton, Erlend Eriksen, Sulev Margus, Henrik T Sørensen, Per H Nielsen, Matti Niemelä, Kari Kervinen, Jens F Lassen, Michael Maeng, Keith Oldroyd, Geoff Berg, Simon J Walsh, Colm G Hanratty, Indulis Kumsars, Peteris Stradins, Terje K Steigen, Ole Fröbert, Alastair NJ Graham, Petter C Endresen, Matthias Corbascio, Olli A Kajander, Uday Trivedi, Juha Hartikainen, Vesa Anttila, David Hildick–Smith, Leif Thuesen, and Evald H Christiansen

On behalf of the NOBLE investigators

NOBLE Trial Design

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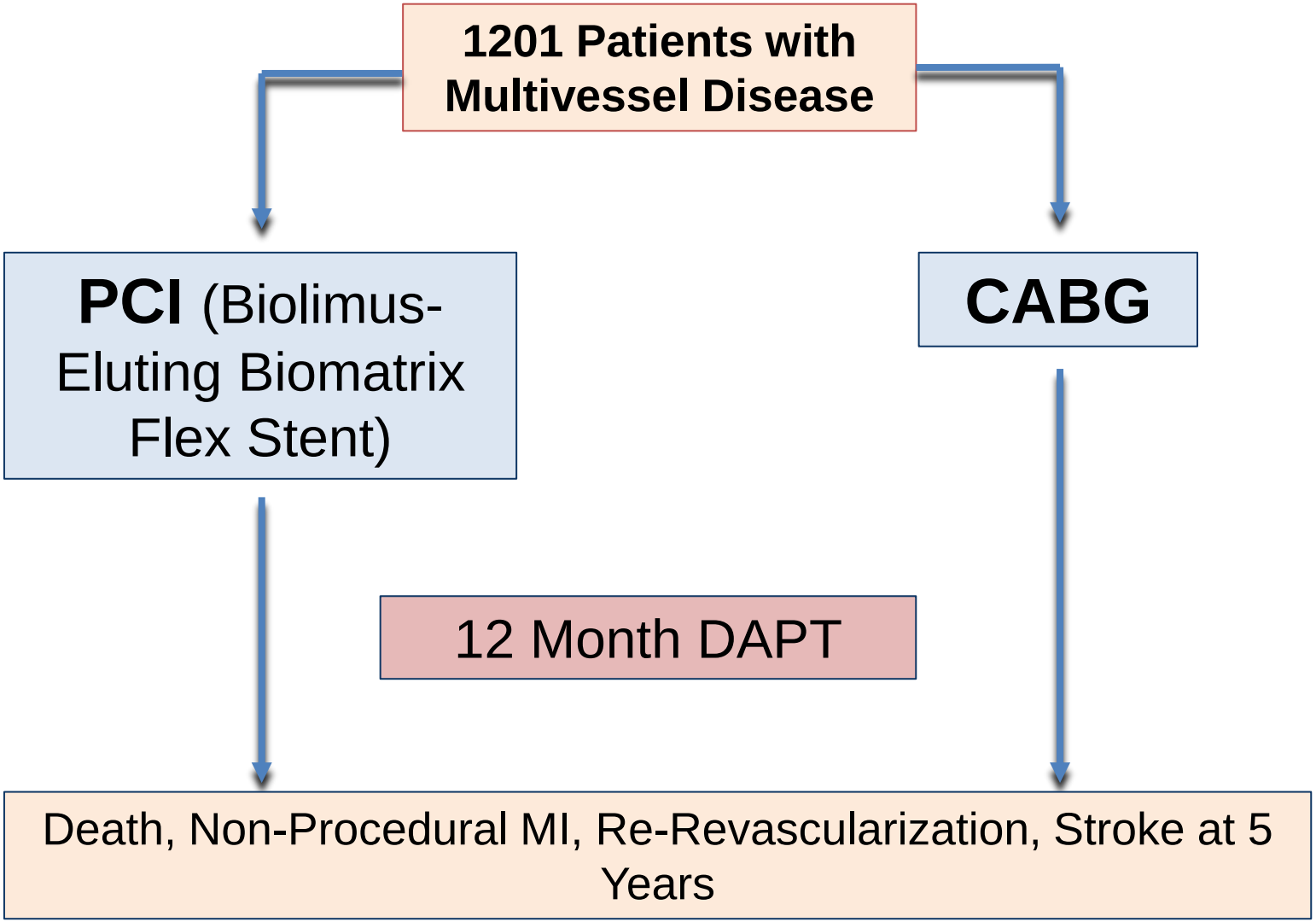

NOBLE Trial Design

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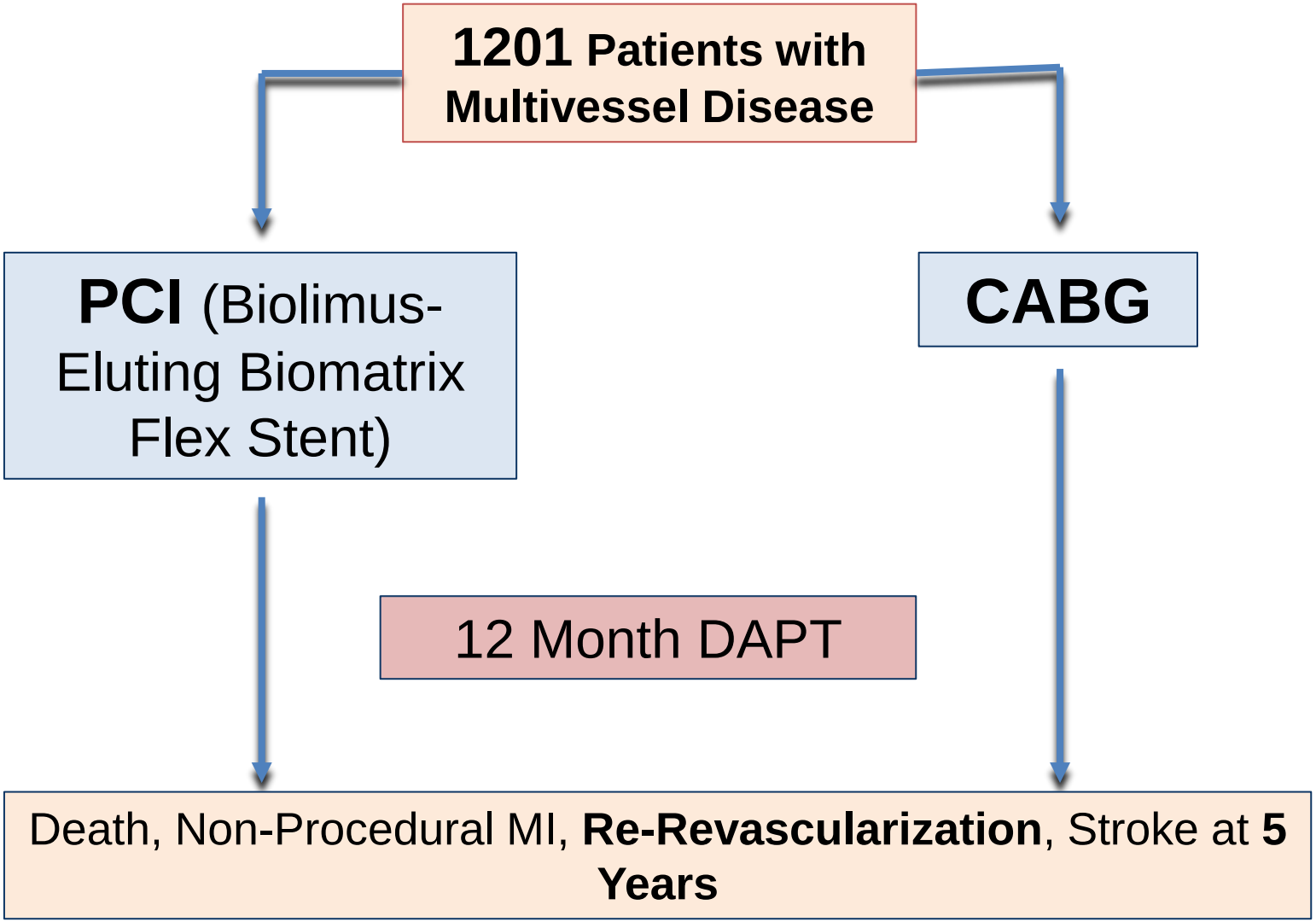
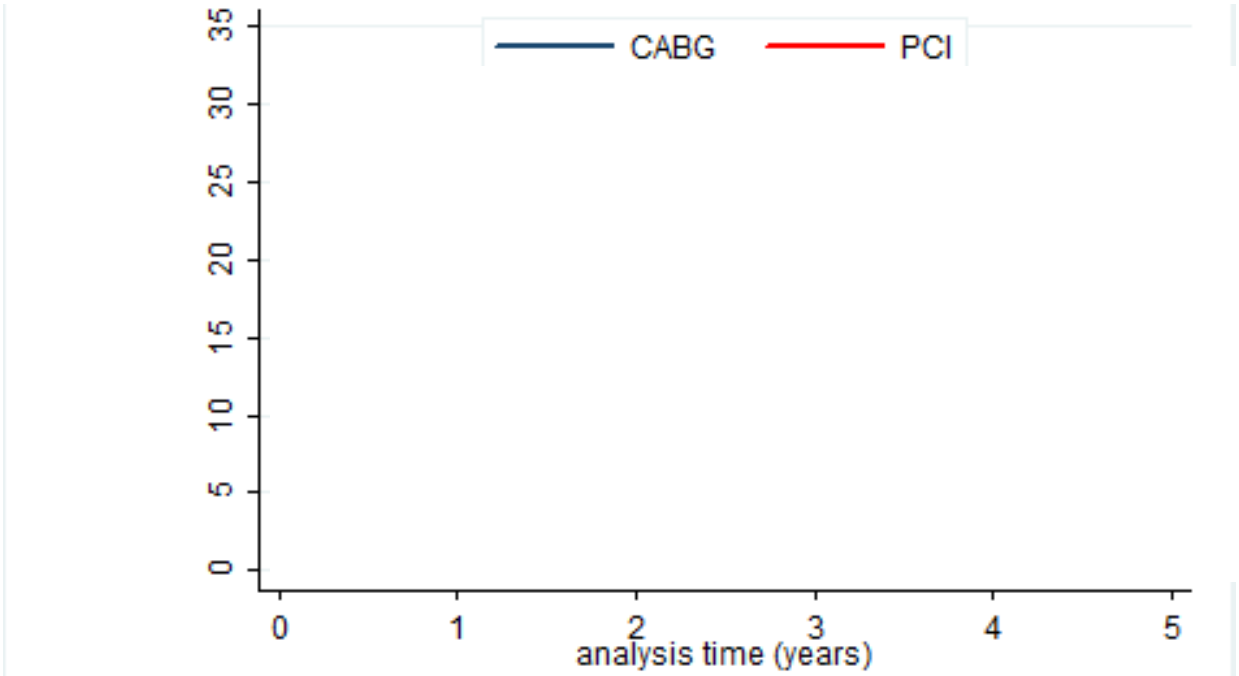


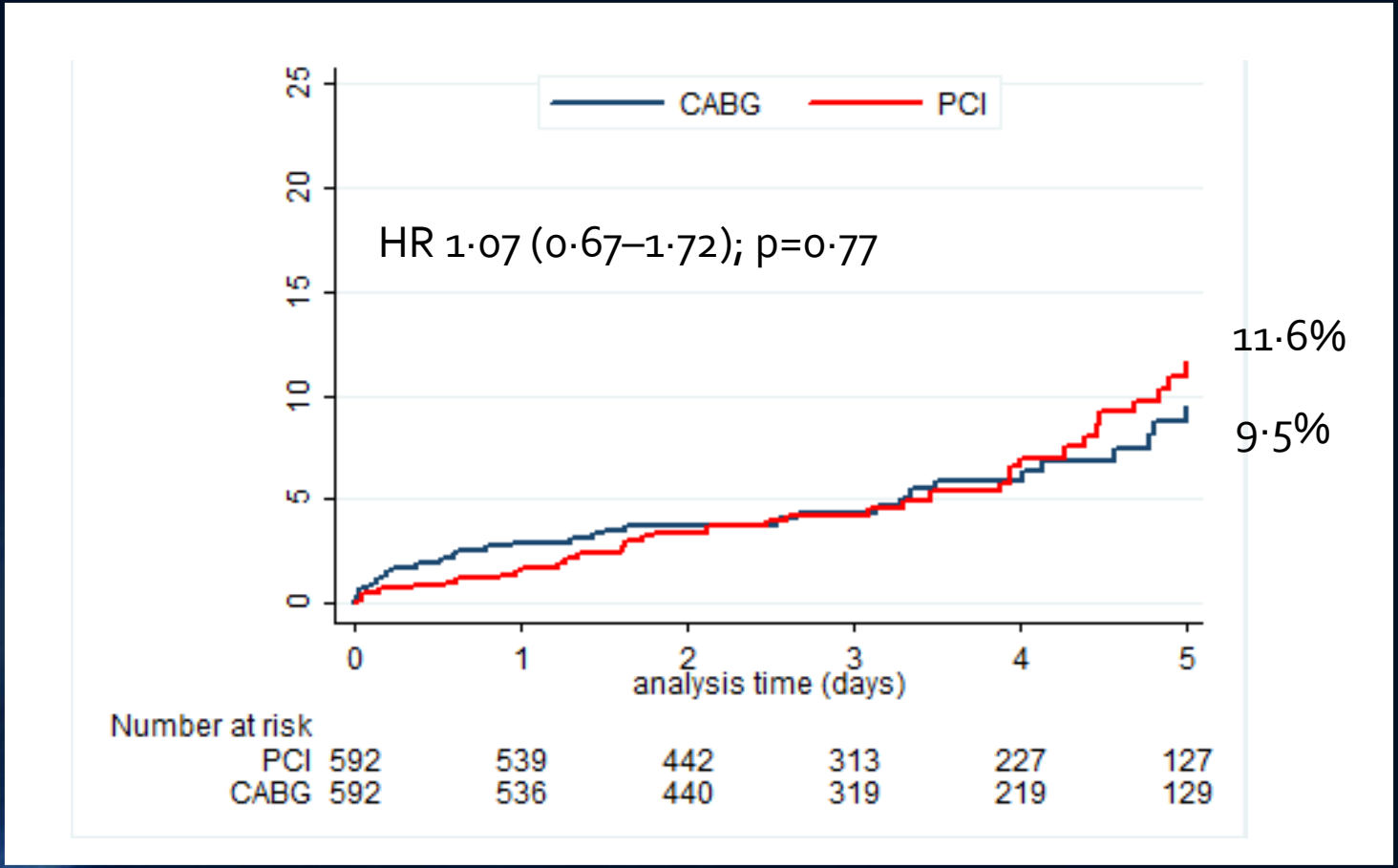
Results
Primary endpoint: MACCE



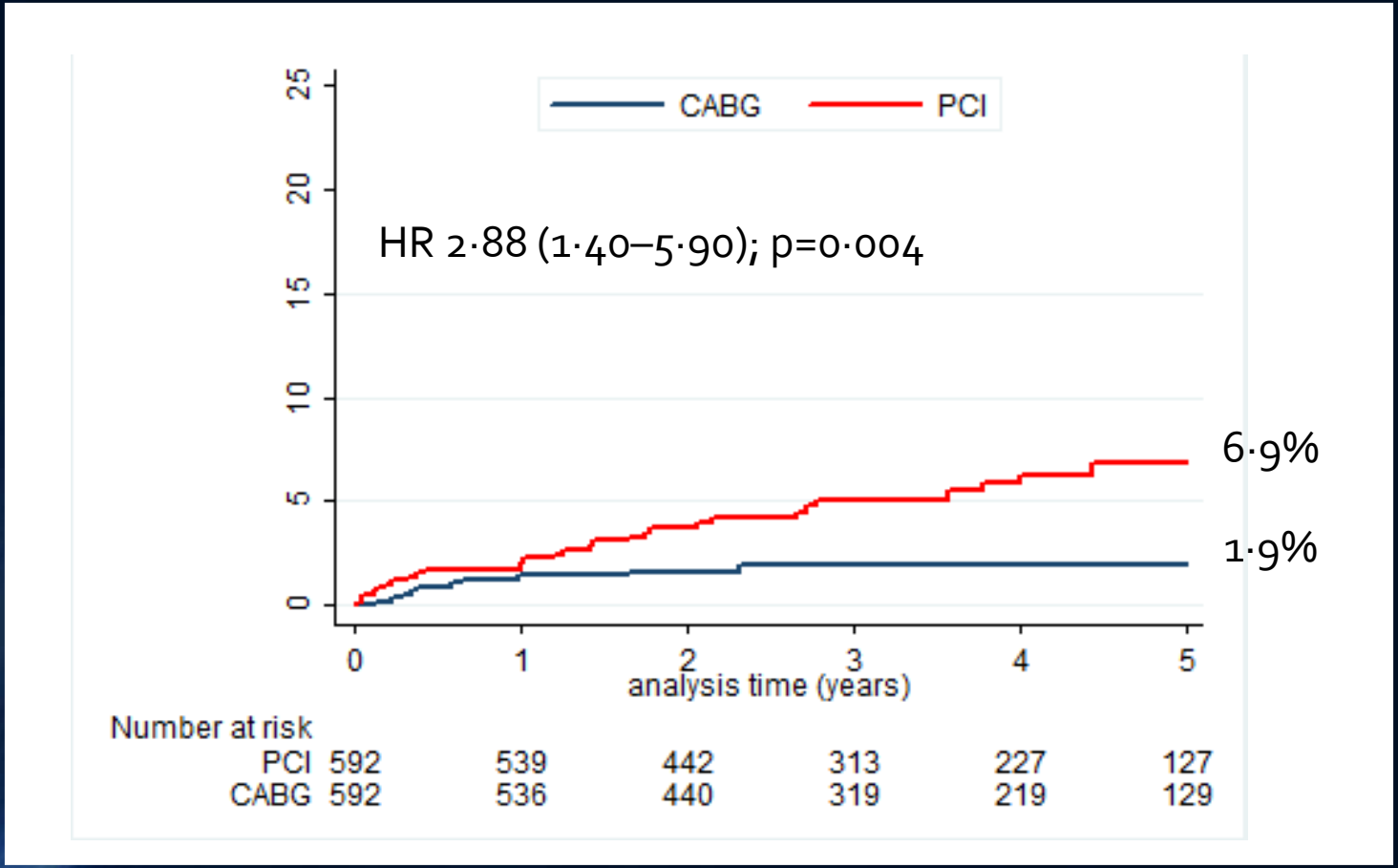
PCI did <u>not</u> show non-inferiority and CABG was superior to PCI

NOBLE

Results
All-cause mortality



Results
Non-procedural myocardial infarction



Results
Secondary endpoints

	PCI	CABG	P–value
Definite ST or symptomatic graft occlusion*	**3%(9)**	**4%(15)**	**0·22**
Procedural myocardial infarction (post hoc)	5%(16/296)	7%(16/238)	0·52

*Kaplan-Meier 5 year estimates by intention-to-treat

Bioabsorbable Scaffolds in PCI: *Background*

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- Absorb stent: 150 μm poly(L-lactide) scaffold + 7μm poly(D,L lactide) coating which elutes everolimus.
- Prior prospective studies were small (ABSORB II – 501 pts, EVERBIO II - 240, ABSORB Japan – 400)
- Concern about late scaffold thrombosis (GHOST-EU Registry) reported 2.1% at 6 months

ABSORB III: Time to Event Analysis

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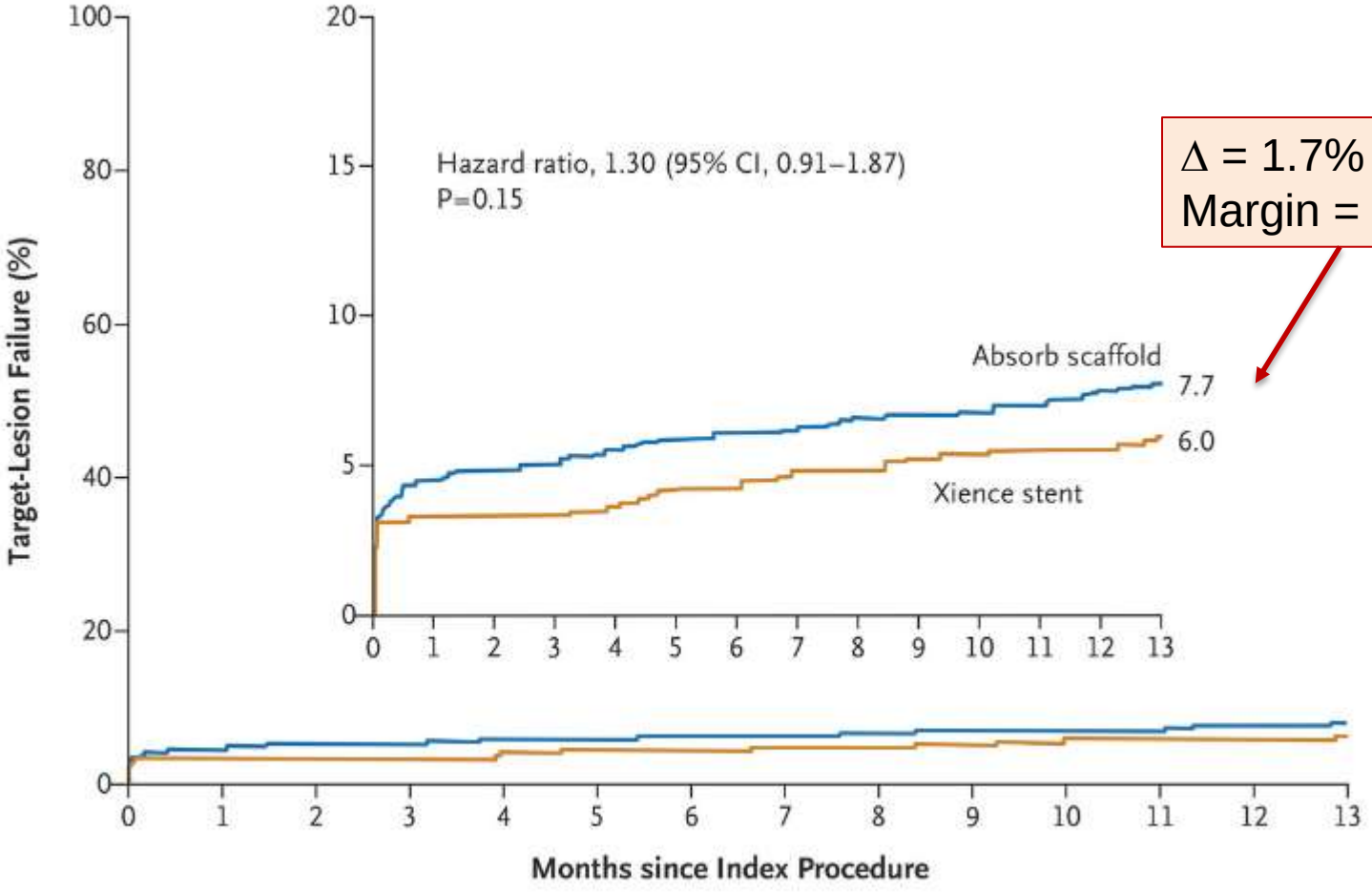
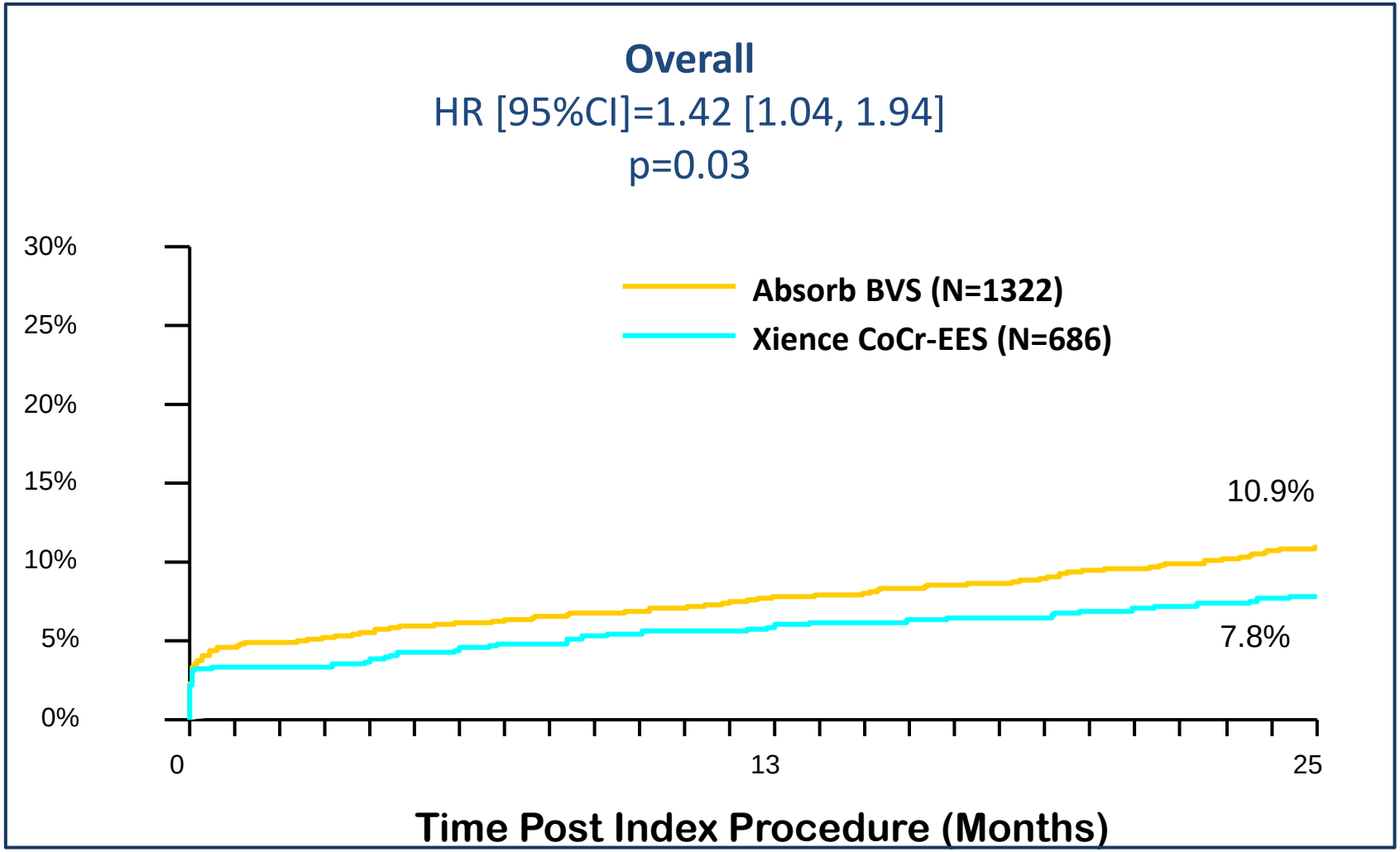


Δ = 1.7%
Margin = 3.5%

No. at Risk					
Absorb	1322	1254	1230	1218	1205
Xience	686	661	651	643	638

Ellis. NEJM.2015;373:1905

ABSORB III: TLF by 2 Years



ABSORB III

Clinical Endpoints by 2 Years

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	Absorb (N=1322)	XIENCE (N=686)	P-Value
TLF	11.0%	7.9%	0.03
Cardiac Death	1.1%	0.6%	NS
TV-MI	7.3%	4.9%	0.04
ID-TLR	5.3%	4.3%	NS
ST (Def/Prob)	1.9%	0.8%	NS

ABSORB II: Three Year Endpoints

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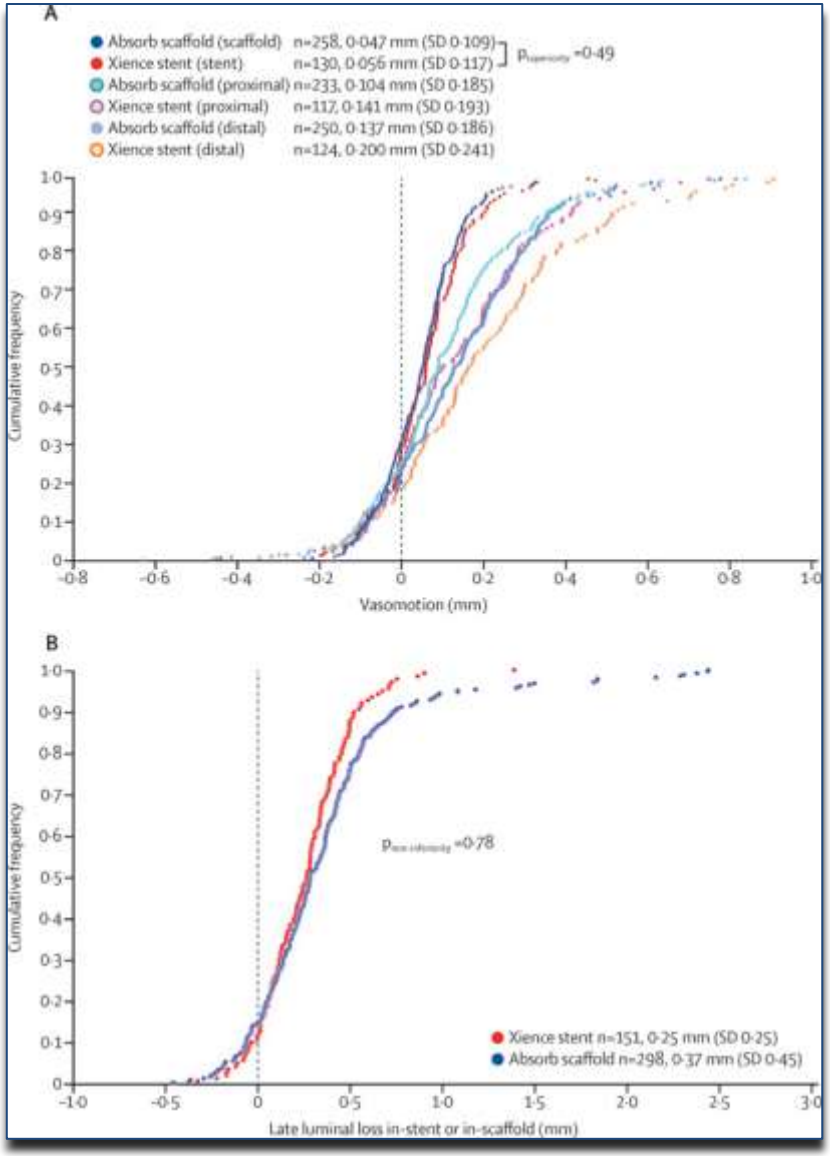

30% of Patients were on DAPT at 3 years

	Absorb	Xience
Cardiac Mortality	3/325 (1%)	3/161 (2%)
Myocardial Infarction	27/325 (8%)	5/161 (3%)
TVR	33/325 (10%)	19/161 (12%)
Very Late Stent or Scaffold Thrombosis	6/329 (2%)	0/164 (0%)

Serruys et al. Lancet. 2016;388:2479

AIDA Trial (All-Comers): Two Year Outcome

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- 1,845 Patients randomized to Absorb vs Xience Stent
- Lesions < 70 mm; no bifurcations allowed
- 63% Post dilation
- 4.5% Non-Inferiority margin for cardiac death, MI, TVR

	BBVS	Metal	P
1 EP	11.1%	10.7%	0.43
Definite ST	3.1%	0.6%	<0.001
Definite or Probable ST	3.5%	0.9%	<0.001

No relation between ST and vessel size, post-dilation, or stent sizing

Wykrzykowska. NEJM. 2017;DOI:10.1056/NEJMoa1614954

FDA Informational Posting

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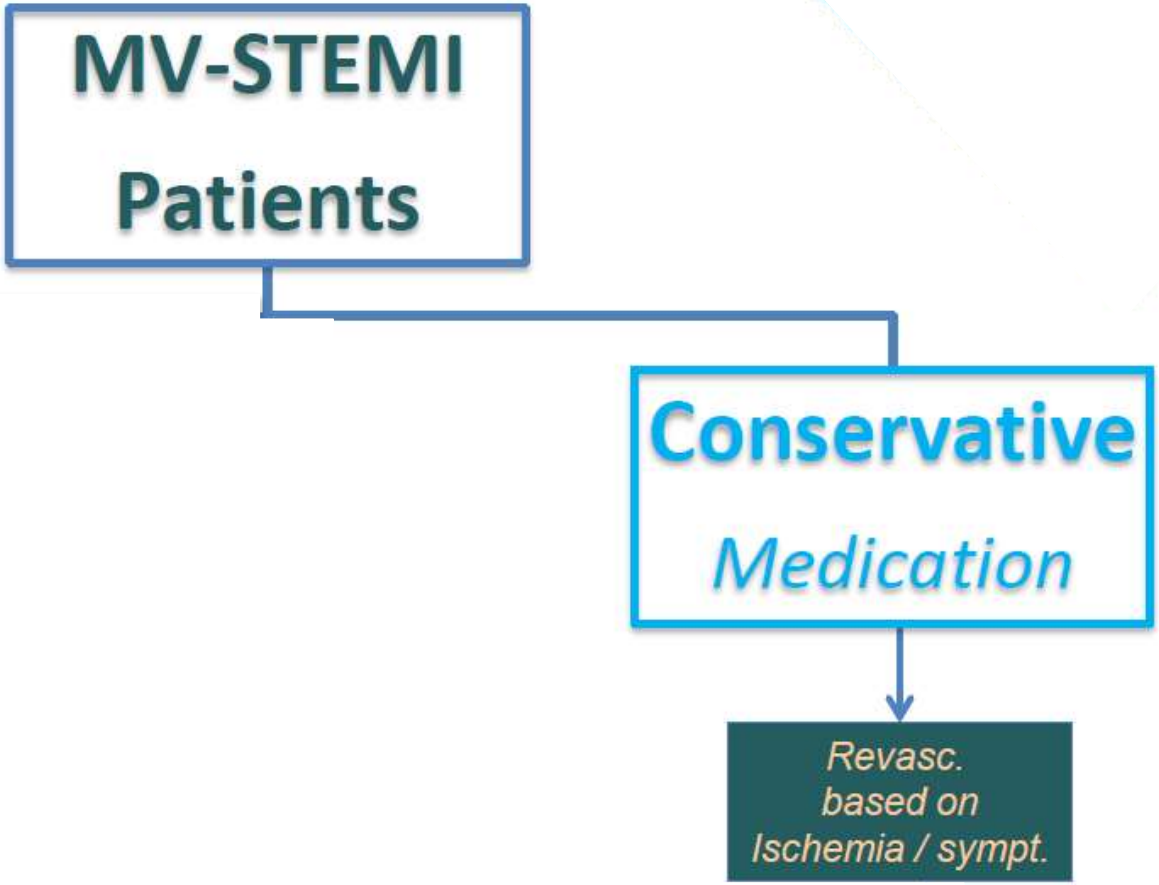
[Posted 03/18/2017]

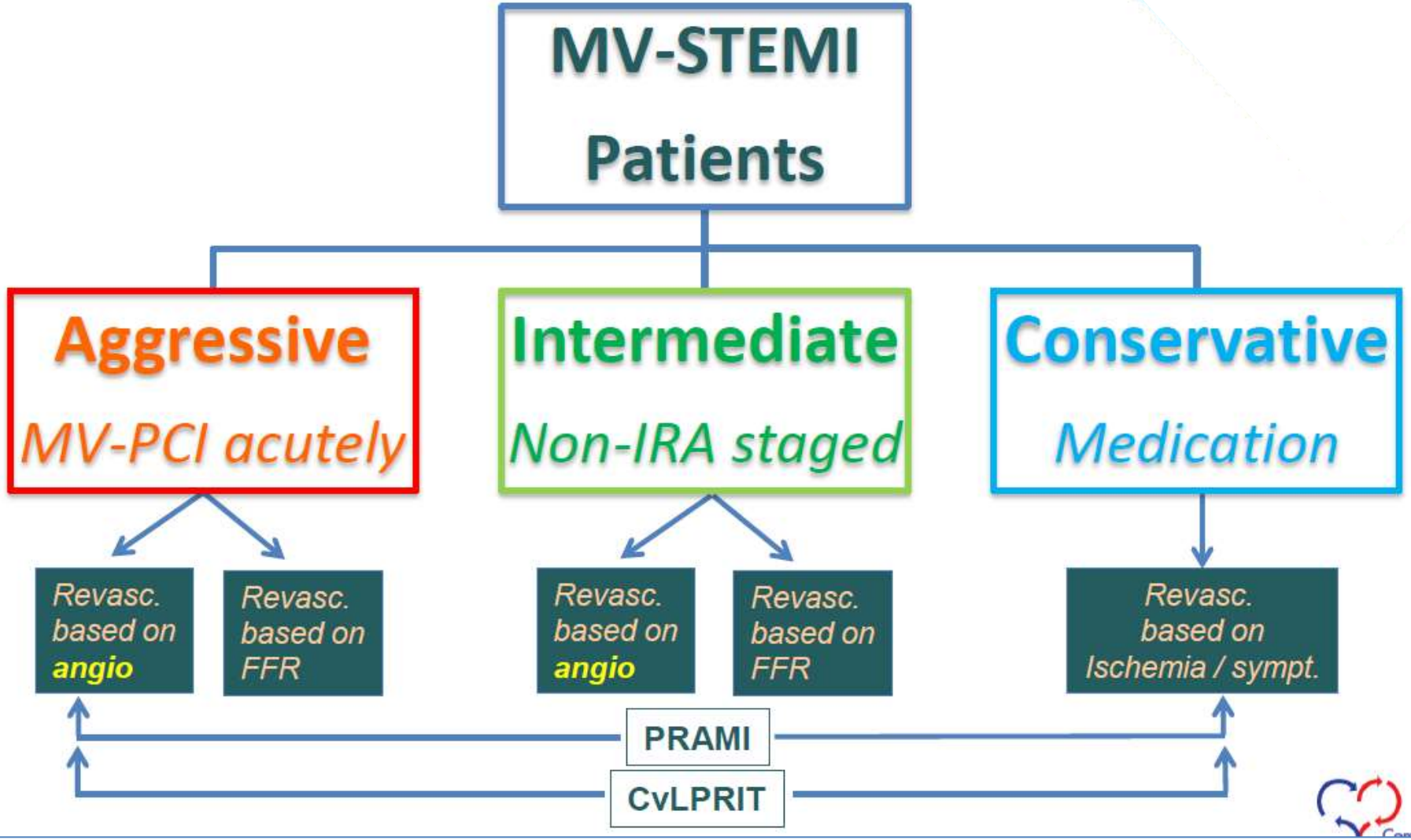
AUDIENCE: Cardiology, Surgery, Risk Manager

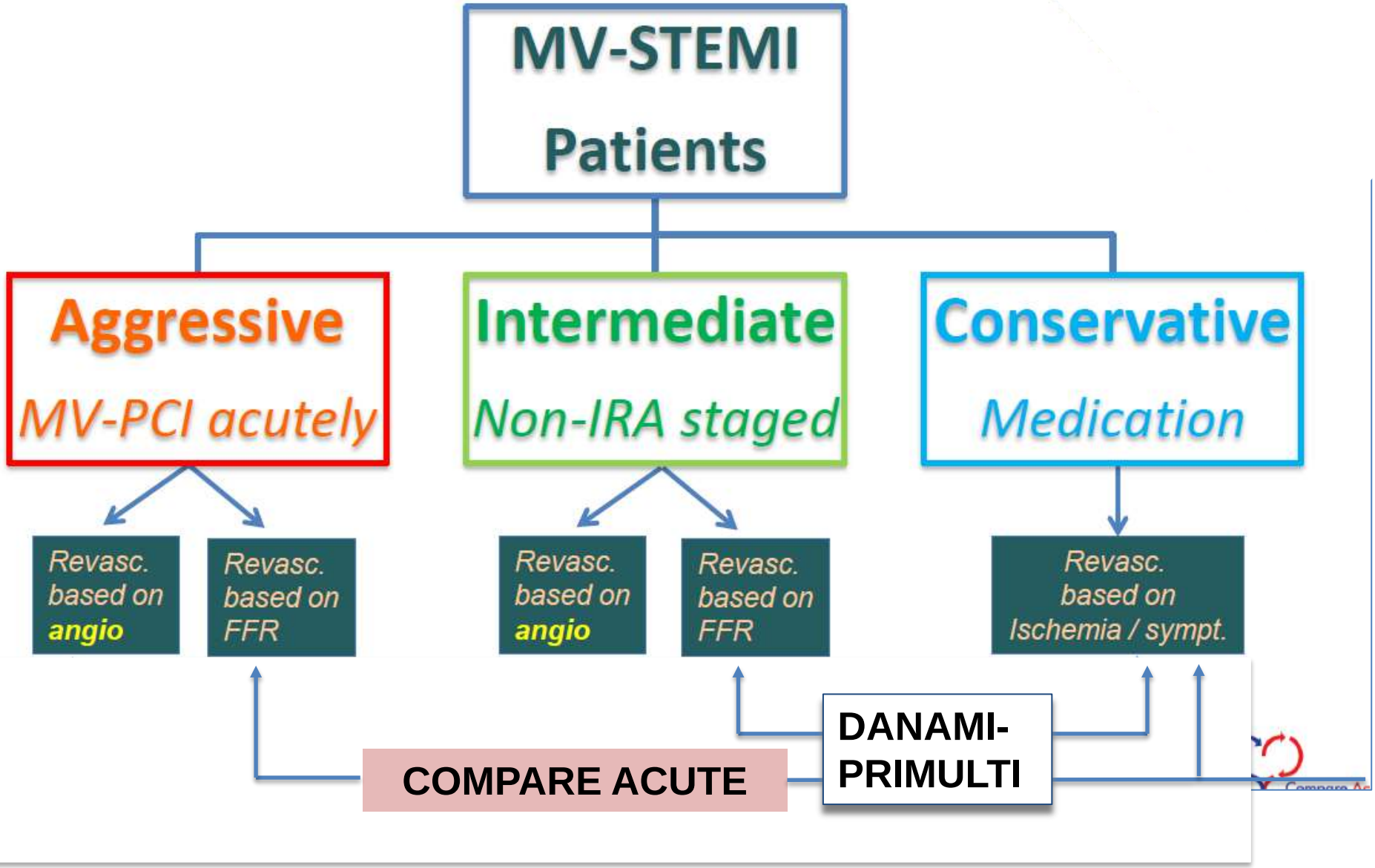
ISSUE: The FDA is informing health care providers treating patients with Absorb GT1 Bioresorbable Vascular Scaffold (BVS) that there is an increased rate of major adverse cardiac events observed in patients receiving the BVS, when compared to patients treated with the approved metallic XIENCE drug-eluting stent.

The FDA's initial review of two-year data from the BVS pivotal clinical study (the ABSORB III trial) shows an 11 percent rate of major adverse cardiac events (e.g., cardiac death, heart attack, or the need for an additional procedure to re-open the treated heart vessel) in patients treated with the BVS at two years, compared with 7.9 percent in patients treated with the already-approved Abbott Vascular's metallic XIENCE drug-eluting stent (p = 0.03). This study also shows a 1.9 percent rate of developing blood clots (thrombosis) within the BVS versus 0.8 percent within the XIENCE stent at 2 years. These observed higher adverse cardiac event rates in BVS patients were more likely when the device was placed in small heart vessels.

https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm547256.htm


MV-STEMI
Patients
Conservative
Medication
Revasc.
based on
Ischemia / sympt.


MV-STEMI Patients
Aggressive
MV-PCI acutely
Intermediate
Non-IRA staged
Conservative
Medication
Revasc. based on angio
Revasc. based on FFR
Revasc. based on angio
Revasc. based on FFR
Revasc. based on Ischemia / sympt.
PRAMI
CvLPRIT


MV-STEMI Patients
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Revasc. based on FFR
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COMPARE ACUTE
DANAMI-PRIMULTI

COMPARE ACUTE

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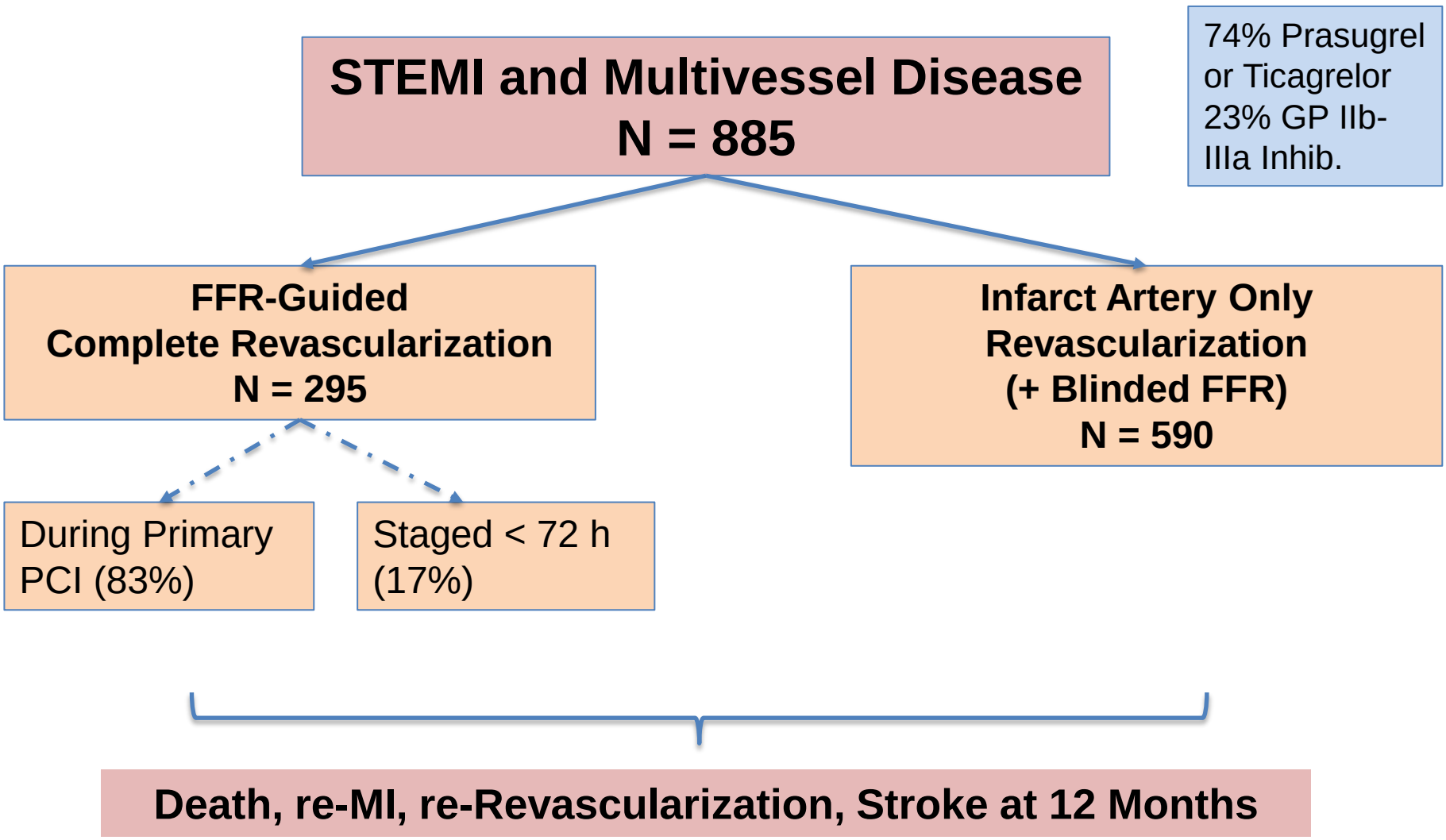

COMPARE ACUTE: Primary Endpoint

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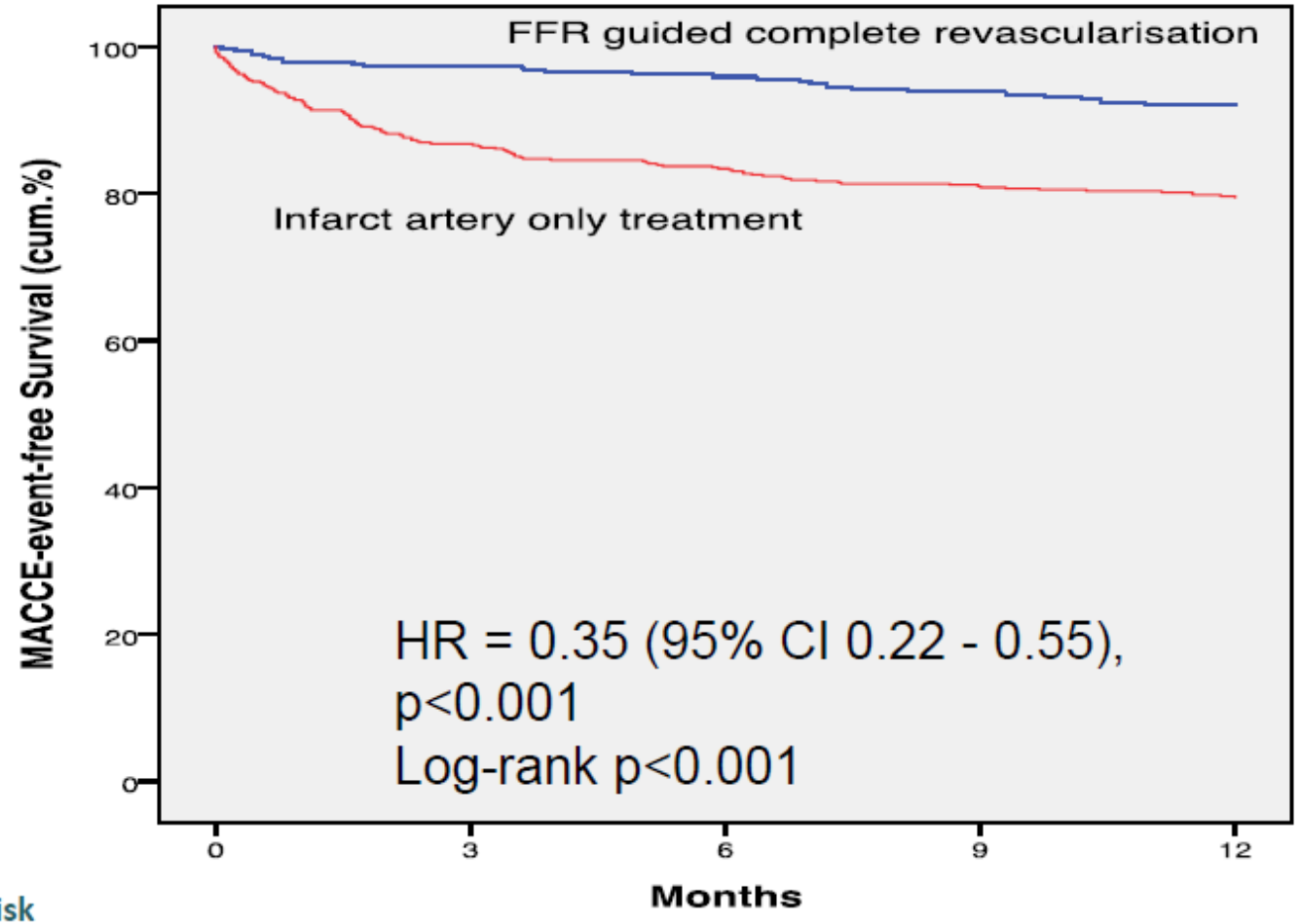

7.8%

20.5%

No. at risk					
FFR guided complete	295	286	281	264	215
Culprit lesion only	590	512	492	457	371

Components of the Primary Endpoint

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	FFR guided Complete Revascularization (n=295)	Infarct Artery Only treatment (n=590)	HR	95% CI	P value
Primary endpoint	Number of events (%)				
MACCE* (any first event)	23 (7.8%)	121 (20.5%)	0.35	0.22 – 0.55	<0.001
Death, all cause	4 (1.3%)	10 (1.7%)	0.80	0.25 – 2.56	0.70
Cardiac	3 (1.0%)	6 (1.0%)			
Myocardial infarction (MI)	7 (2.4%)	28 (4.7%)	0.50	0.22 - 1.13	0.10
Spontaneous	5 (1.6%)	17 (2.9%)	0.59	0.22 – 1.59	0.29
Peri-procedural	2 (0.6%)	11 (1.9%)	0.36	0.08 – 1.64	0.19
Revascularization	18 (6.1%)	103 (17.5%)	0.32	0.20 – 0.54	<0.001
PCI	15 (5.1%)	98 (16.6%)	0.37	0.24 – 0.57	<0.001
CABG	3 (1.0%)	5 (0.8%)	1.20	0.29 – 5.02	0.80
Cerebrovascular event	0 (0.0%)	4 (0.7%)	NA	NA	NA

Perspective

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- Complete revascularization has almost always proven superior to incomplete revascularization.
- The current trend is to manage stable coronary lesions conservatively.
- FAME 2 suggests that adding FFR may prove a useful discriminator (i.e. stent only the worst lesions).
- The preponderance of evidence now favors a more aggressive approach to non-culprit lesions
- Specific criteria favoring acute NCL PCI aren't yet defined