Thromboseforum 2015

Antithrombozytäre Therapie bei DES und bioresorbierbaren Scaffolds – wie lange DAPT, bei welchen Patienten können wir zukünftig auf Aspirin verzichten?

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Leitender Oberarzt
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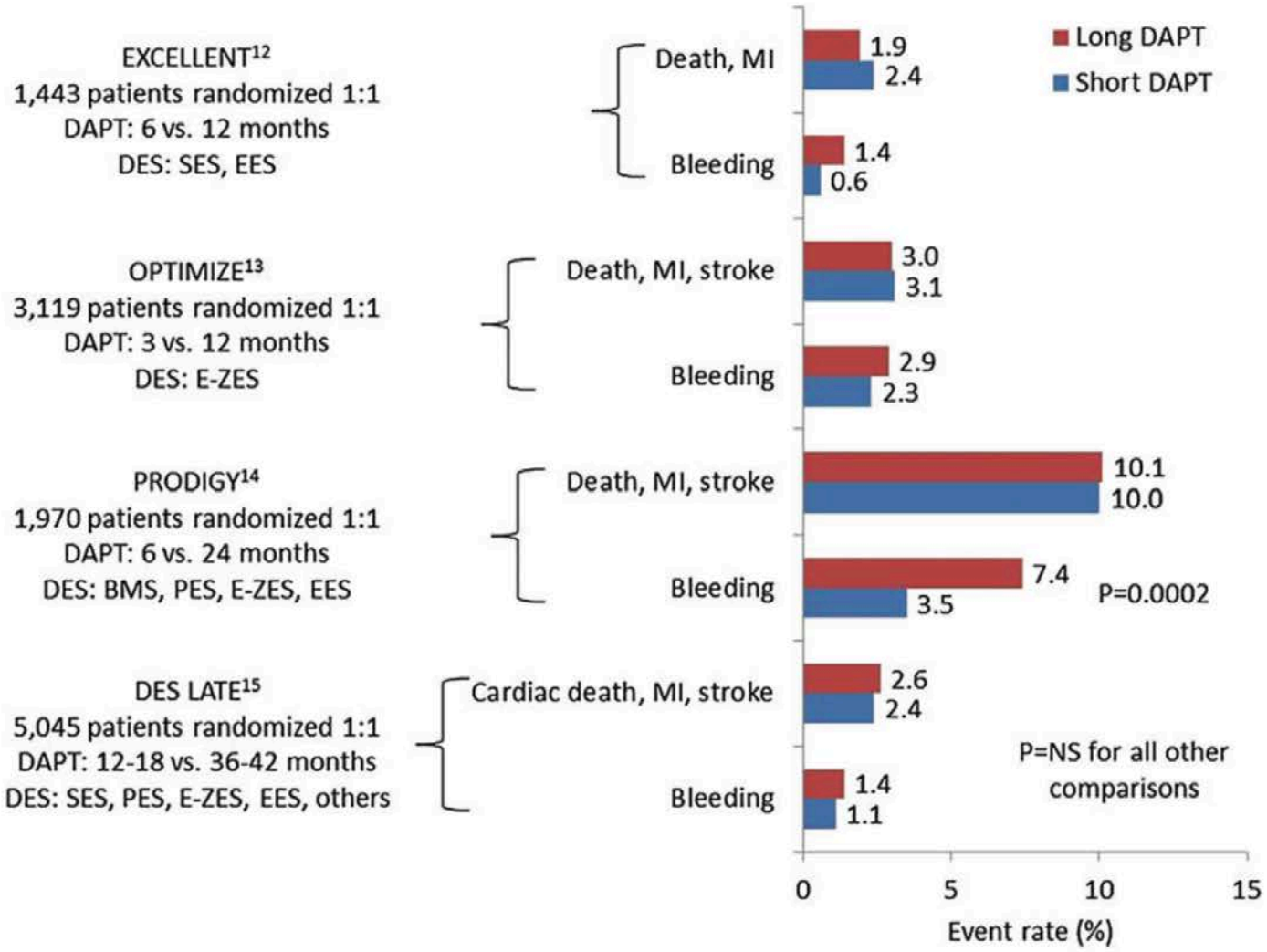
DAPT – wie lange nach Drug-eluting Stent?

- 1-3 Monate
- 6 Monate
- 12 Monate
- 24-30 Monate



Stone, Eur Heart J 2014; 35:1914-1916

Thromboseforum 2015

- **DAPT = dual antiplatelet therapy**
  - Italic
  - ISAR-Safe
  - DAPT

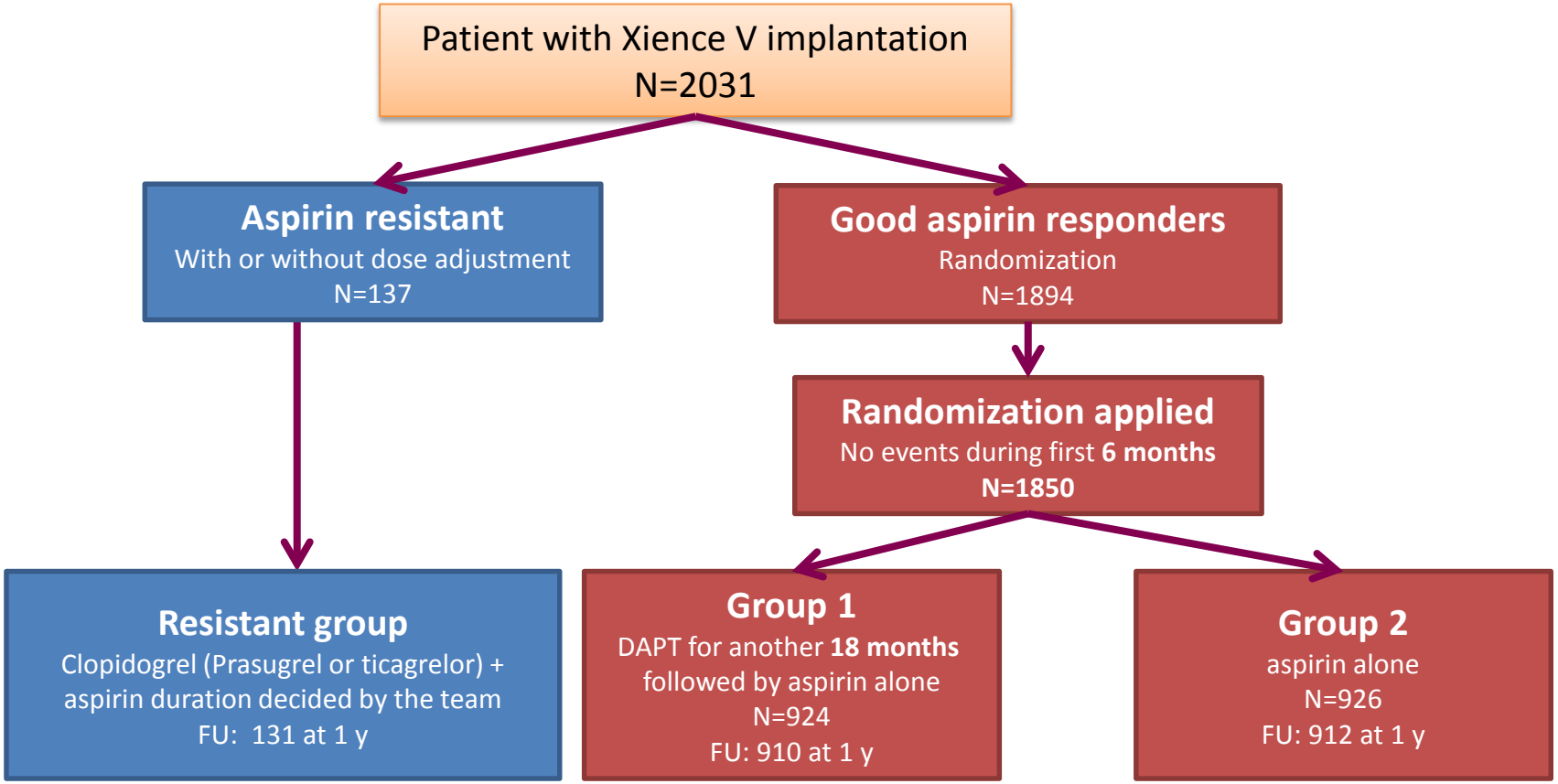
- Scaffold = bioresorbable “stent”

ITALIC

Study flow

Major inclusion criteria

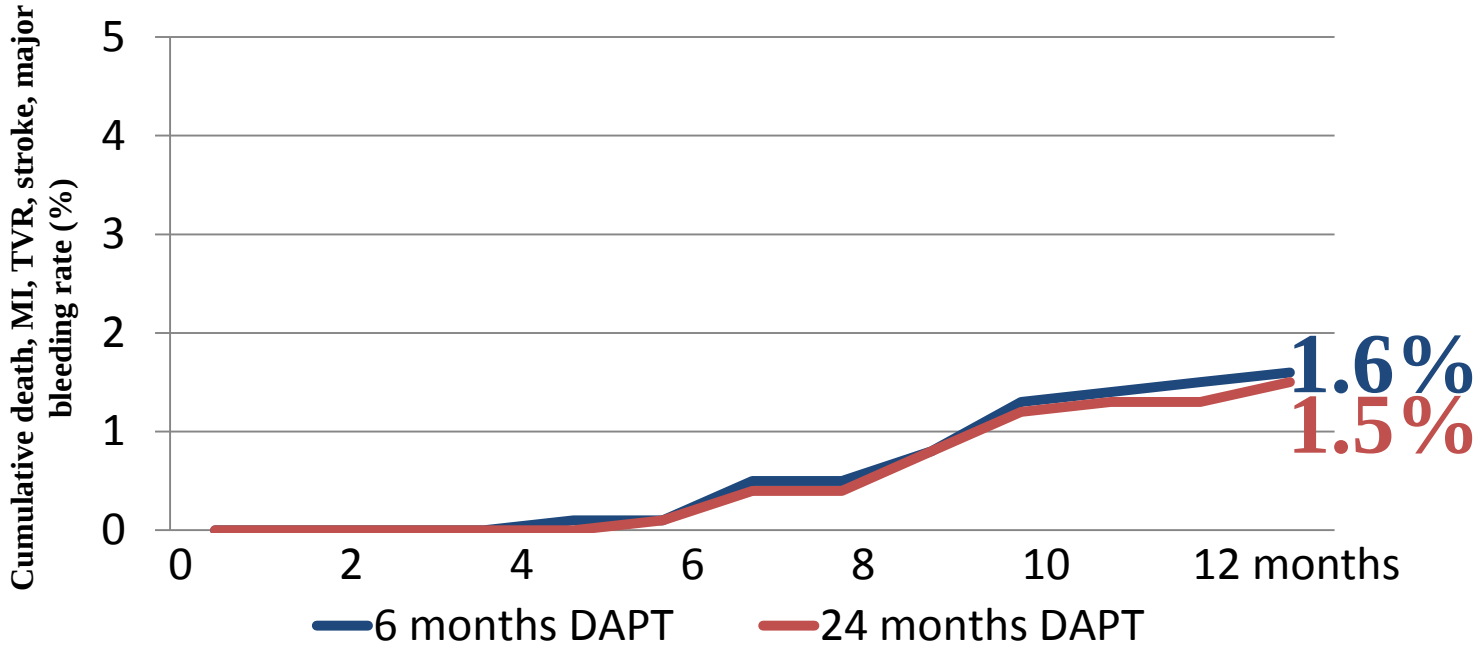
1. Patients > 18 years
2. At least 1 Xience V DES implanted
3. Not pretreated with abciximab
4. Exclusion of aspirin resistance



Gilard M et al., AHA 2014; J Am Coll Cardiol. 2014 Nov 16

ITALIC

Primary endpoint



24 months DAPT	910	910	910	910	905	901	896
6 months DAPT	912	912	912	911	905	900	897

→ Non-inferiority was established for 6 month vs. 24 month DAPT

Six versus Twelve Months of Clopidogrel Therapy After Drug-Eluting Stenting

– the Randomized, Double-Blind, Placebo-Controlled ISAR-SAFE Trial

Stefanie Schulz-Schüpke, Julinda Mehilli, Karl-Ludwig Laugwitz, Franz-Josef Neumann, Jurrien M ten Berg, Tom Adriaenssens, Yaling Han, Barbara von Merzljak, Gert Richardt, Melchior Seyfarth, Klaus Tiroch, Tanja Morath, Michael Maeng, Bernhard Zrenner, Nonglag Rifatov, Claudius Jacobshagen, Harald Mudra, Eberhard von Hodenberg, Jochen Wöhrle, Sebastian Kufner, Christian Hengstenberg, Marcus Fischer, Martin Schmidt, Franz Dotzer, Tareq Ibrahim, Peter Sick, Christoph A Nienaber, Arnoud W J van 't Hof, Takeshi Kimura, Bernhard Witzenbichler, Stephan Windecker, Heribert Schunkert, Adnan Kastrati

Eur Heart J. 2015 Jan 23. epub

Study Flow

Months after index PCI

0

6

15

DES

Continuous clopidogrel therapy for 6 months

Randomization (n=4005)

6 months Placebo (n=1998)

6 months Clopidogrel (n=2007)

Study therapy not initiated (n=1)
- immediate withdrawal of consent (n=1)

Study therapy not initiated (n=4)
- immediate withdrawal of consent (n=2)
- physician decision due to erroneous enrolment (n=2)

Incomplete 9-month follow-up (n=127)

Premature study drug discontinuation (n=255)

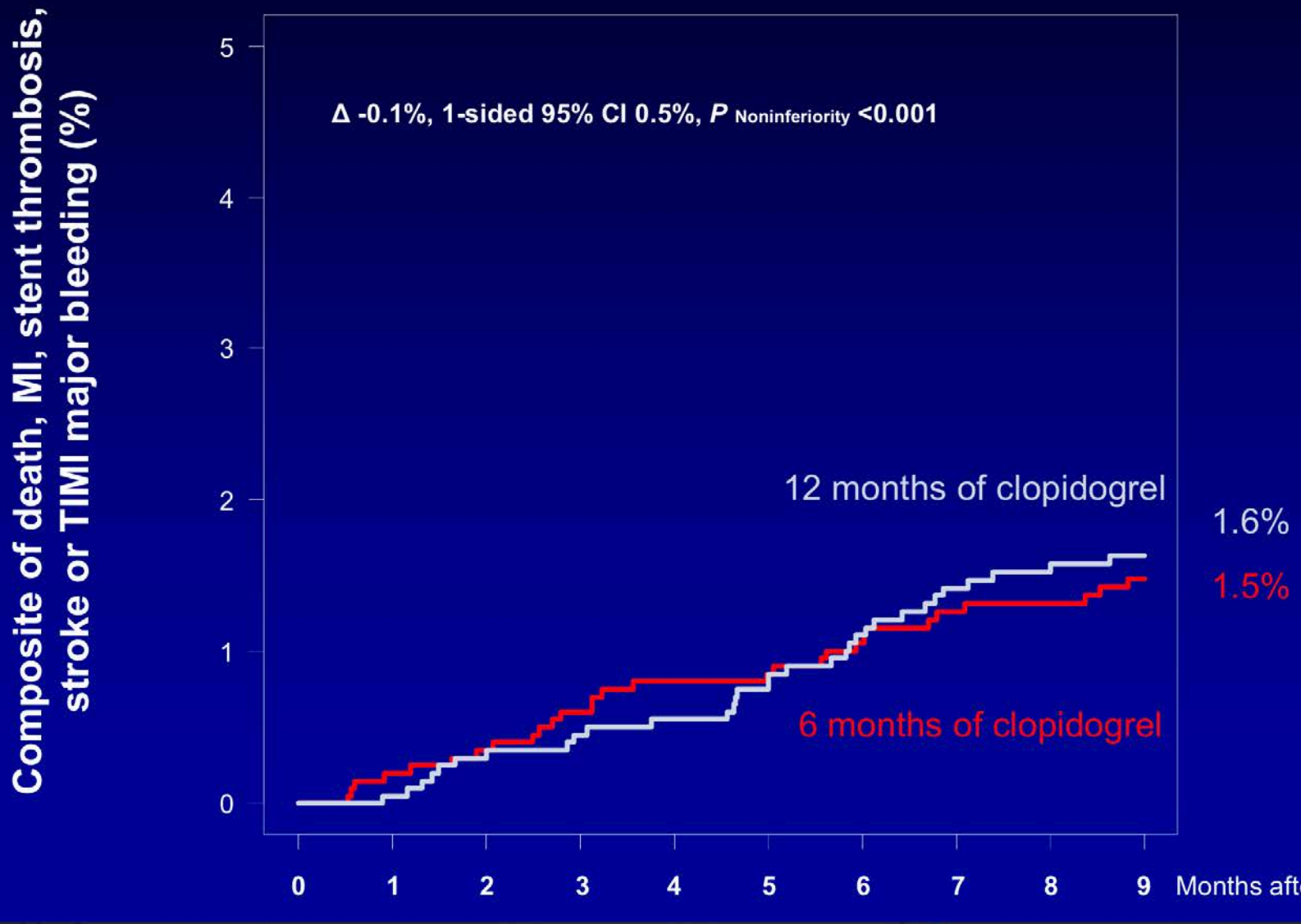
Incomplete 9-month follow-up (n=135)

Premature study drug discontinuation (n=277)

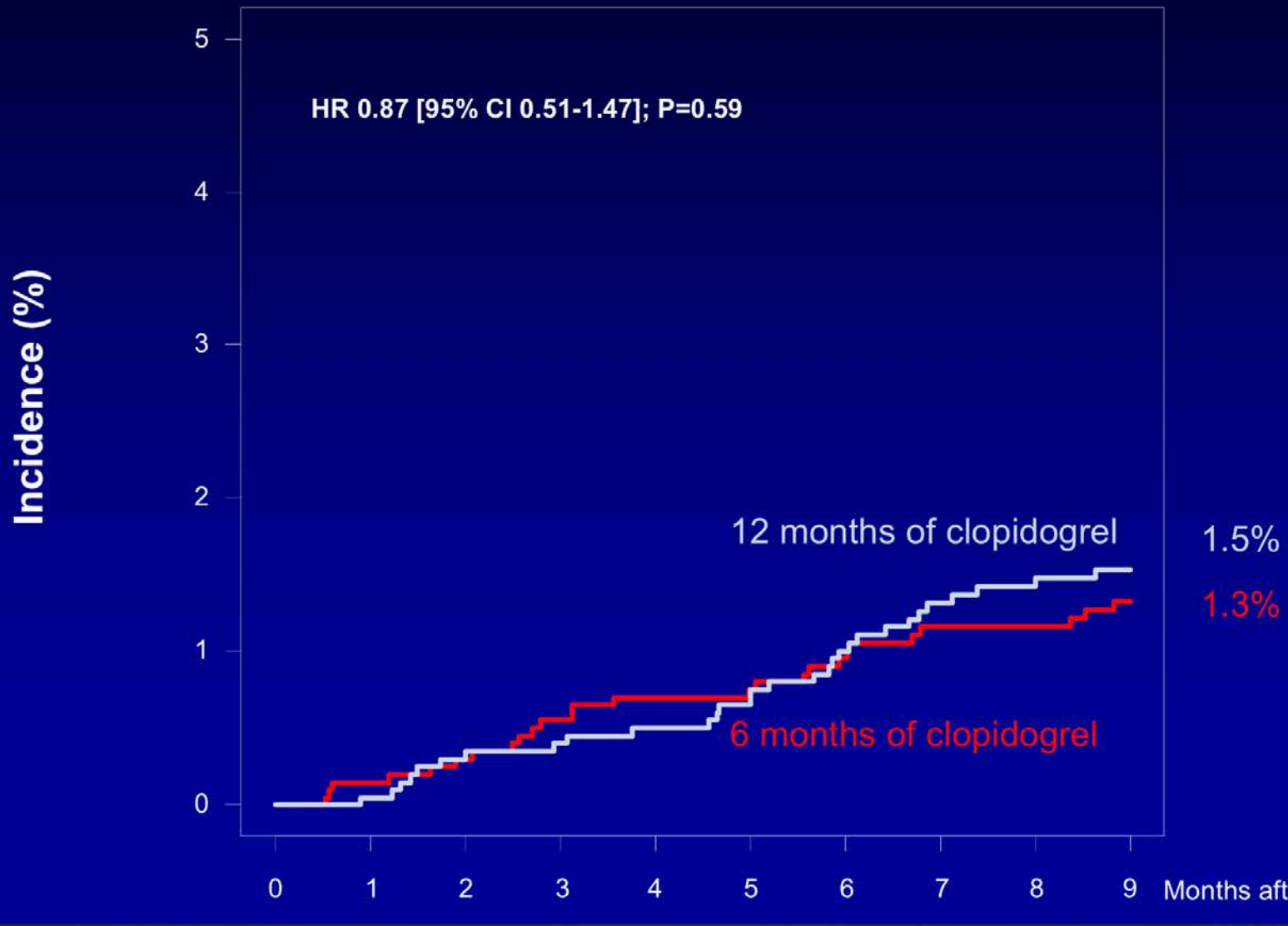
Included for analysis (n=1997)

Included for analysis (n=2003)

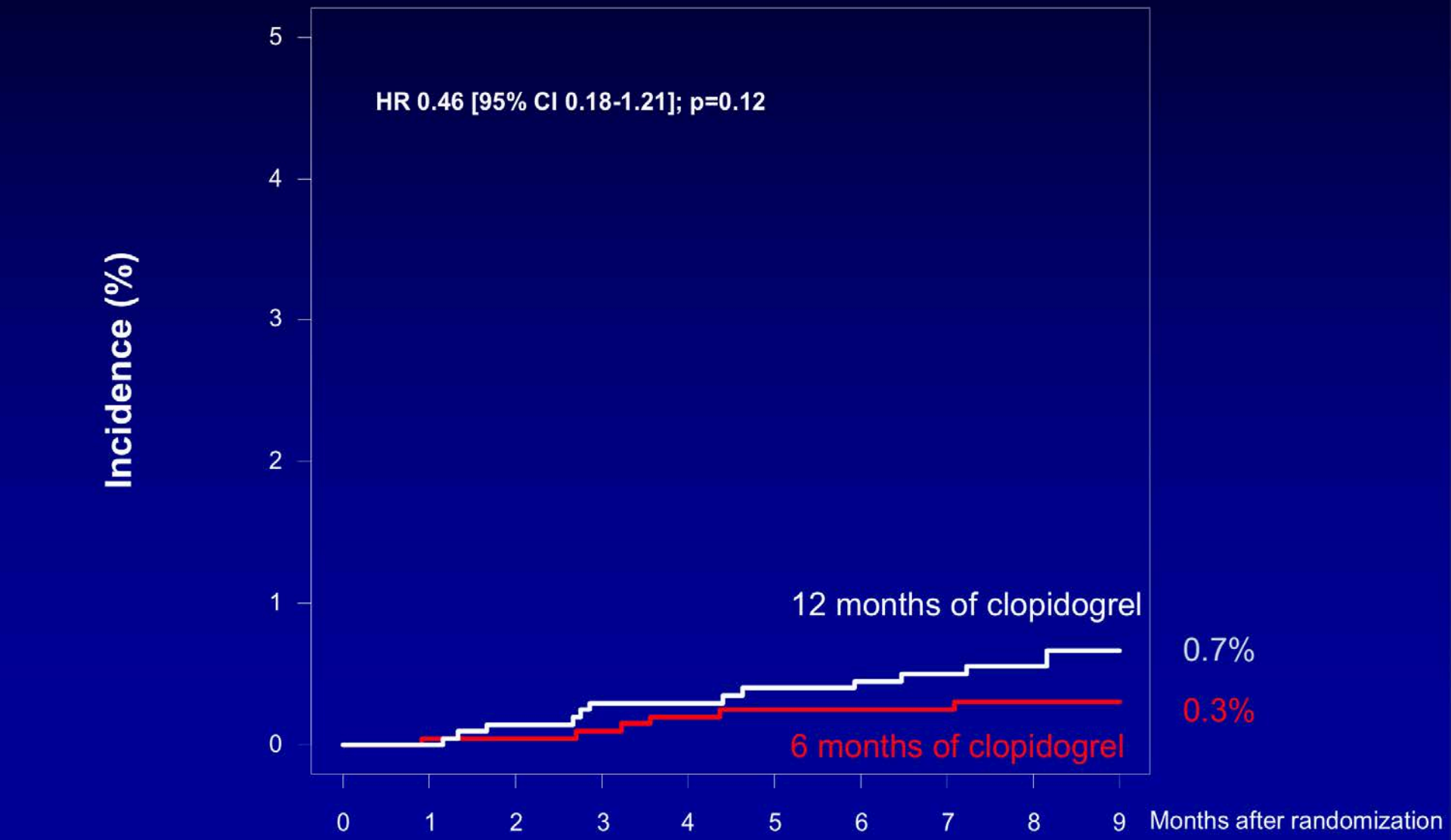
Primary Endpoint



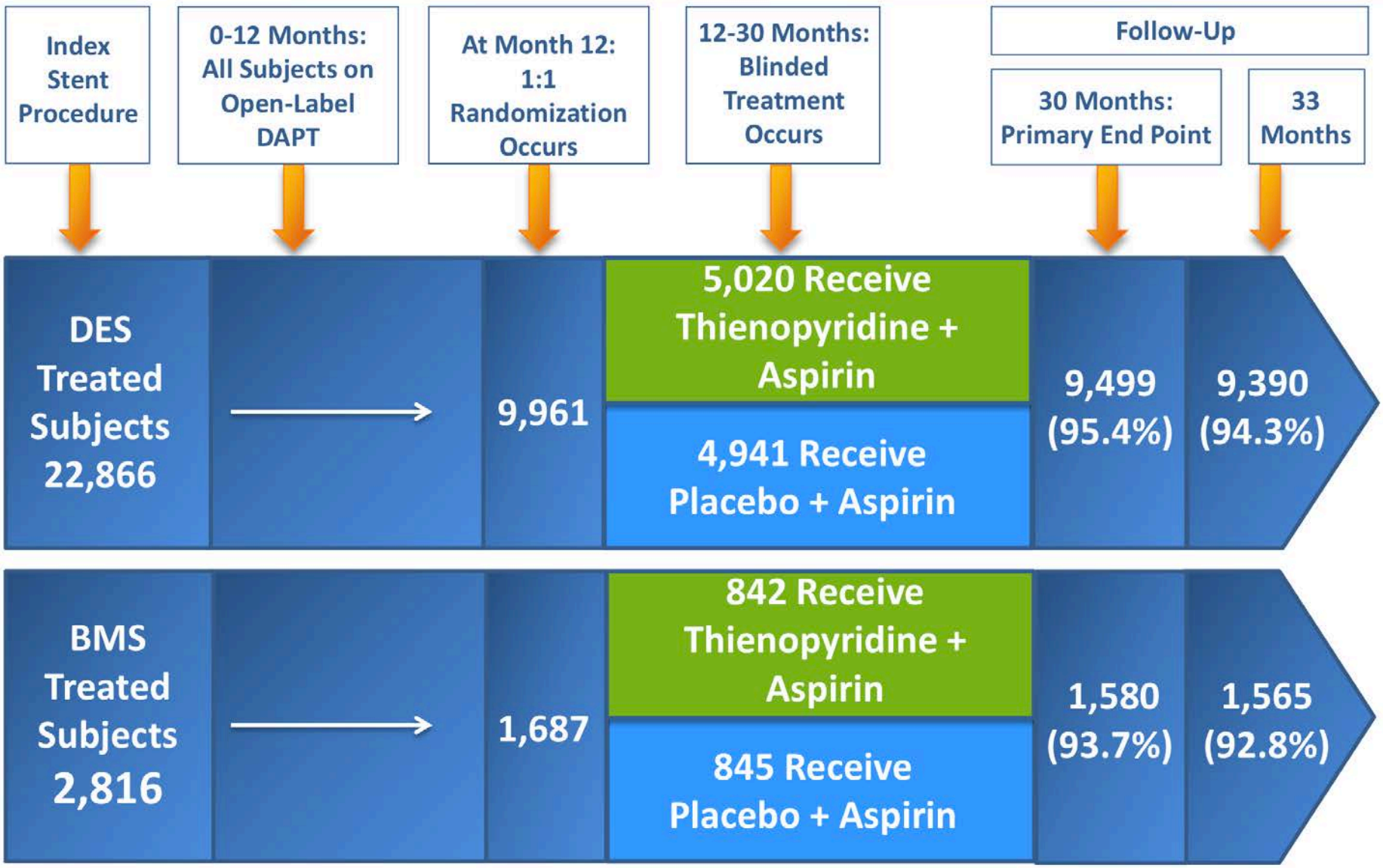
Composite of Death, Myocardial Infarction, Stent thrombosis or Stroke



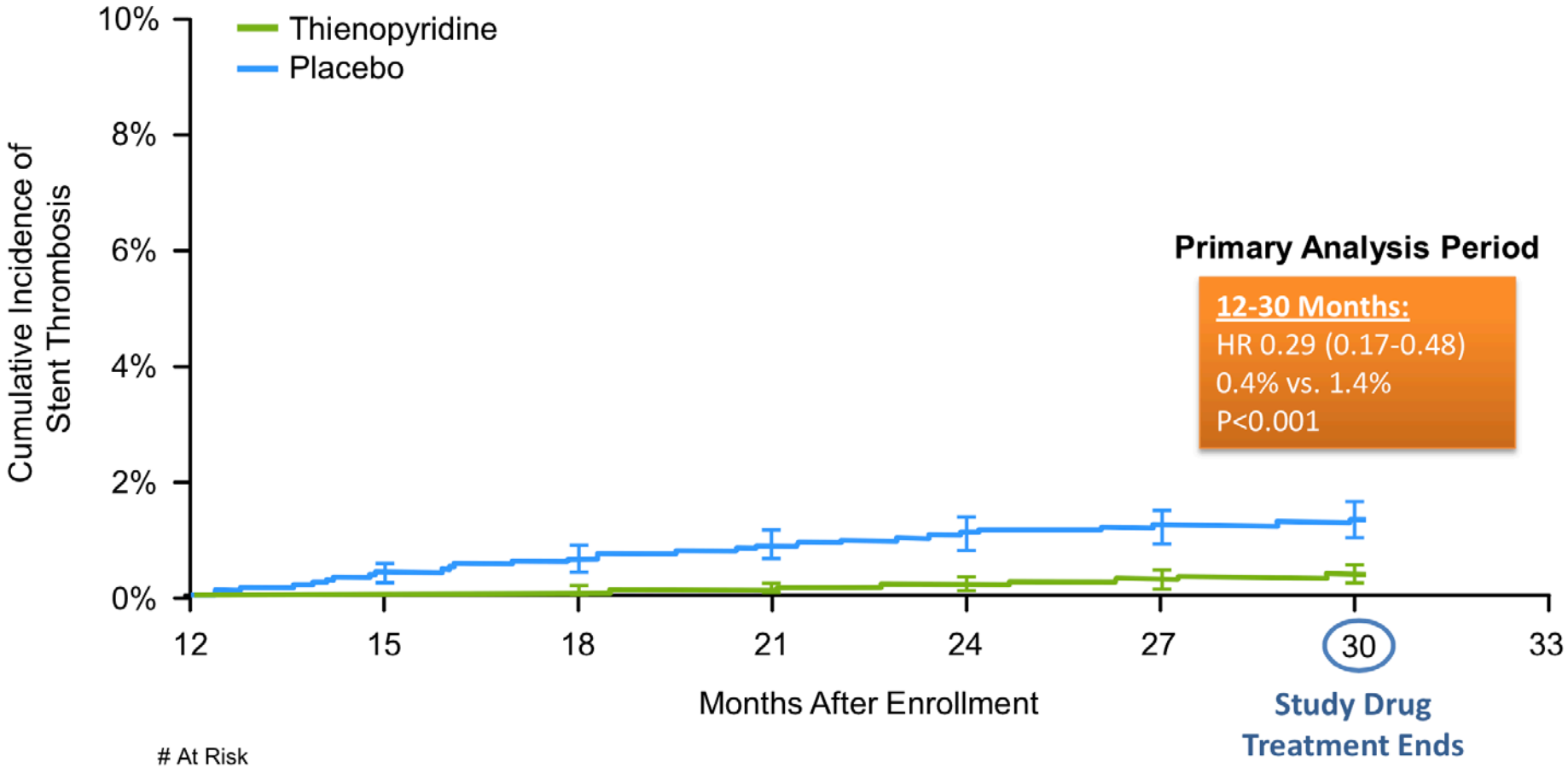
TIMI Major or Minor Bleeding



Subject Flow

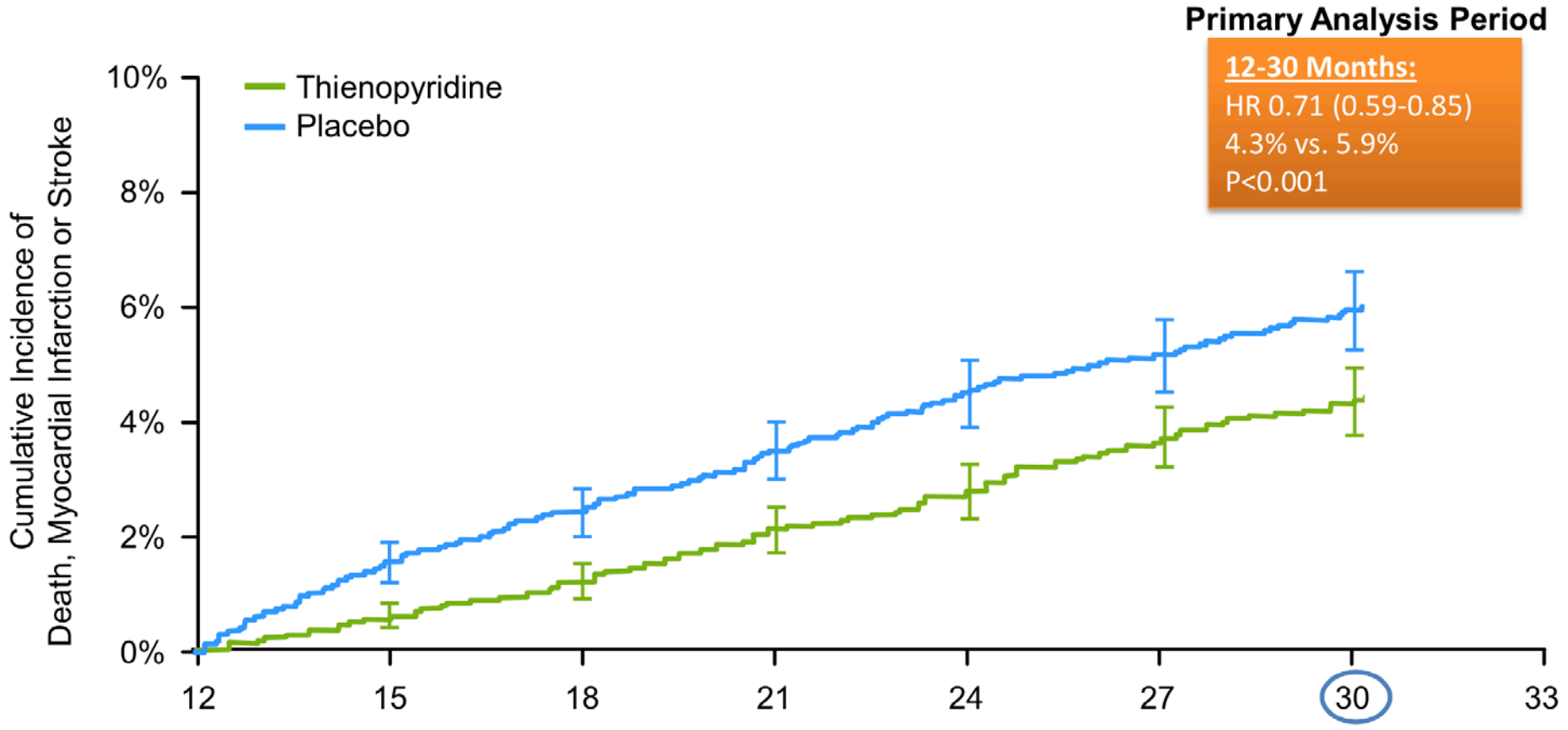


Co-Primary Effectiveness End Point Stent Thrombosis



# At Risk								
Thienopyridine	5020	4934	4870	4828	4765	4686	4642	3110
Placebo	4941	4845	4775	4721	4651	4603	4556	3105

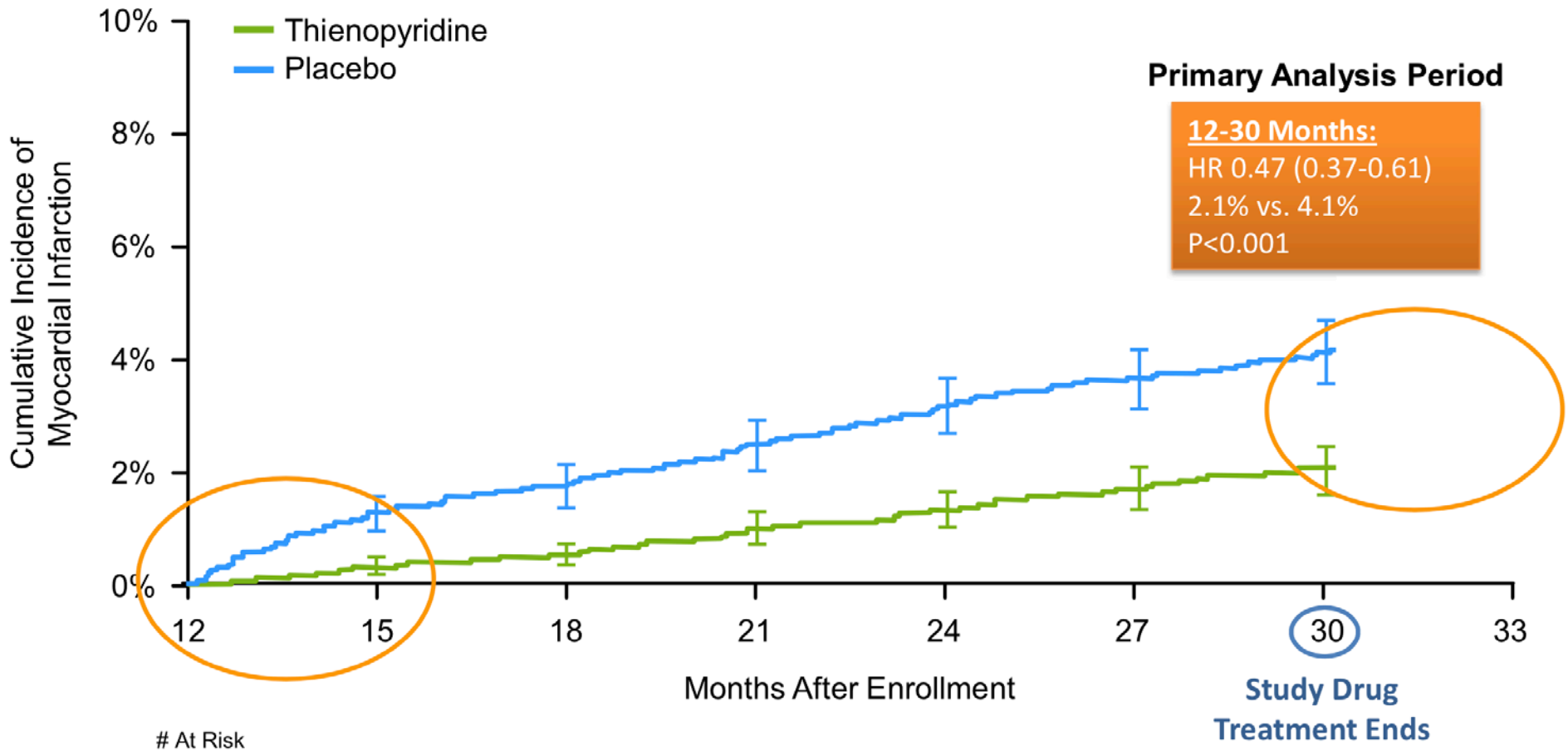
Co-Primary Effectiveness End Point MACCE



# At Risk								
Thienopyridine	5020	4917	4840	4778	4702	4611	4554	3029
Placebo	4941	4799	4715	4635	4542	4476	4412	2997

Myocardial Infarction

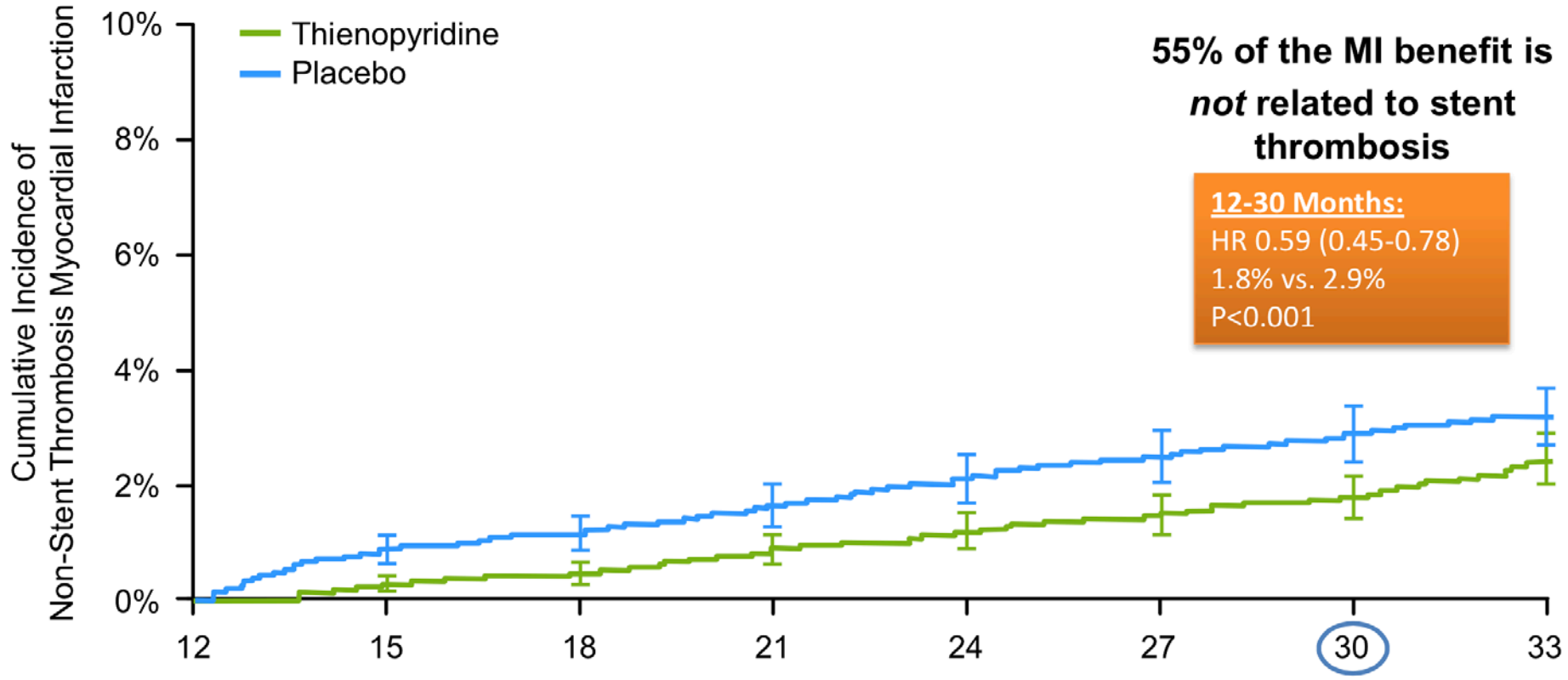
DAPT STUDY



# At Risk								
Thienopyridine	5020	4920	4849	4789	4717	4634	4580	3051
Placebo	4941	4804	4727	4653	4565	4501	4440	3012

Non-Stent Thrombosis Myocardial Infarction

DAPT STUDY



55% of the MI benefit is *not* related to stent thrombosis

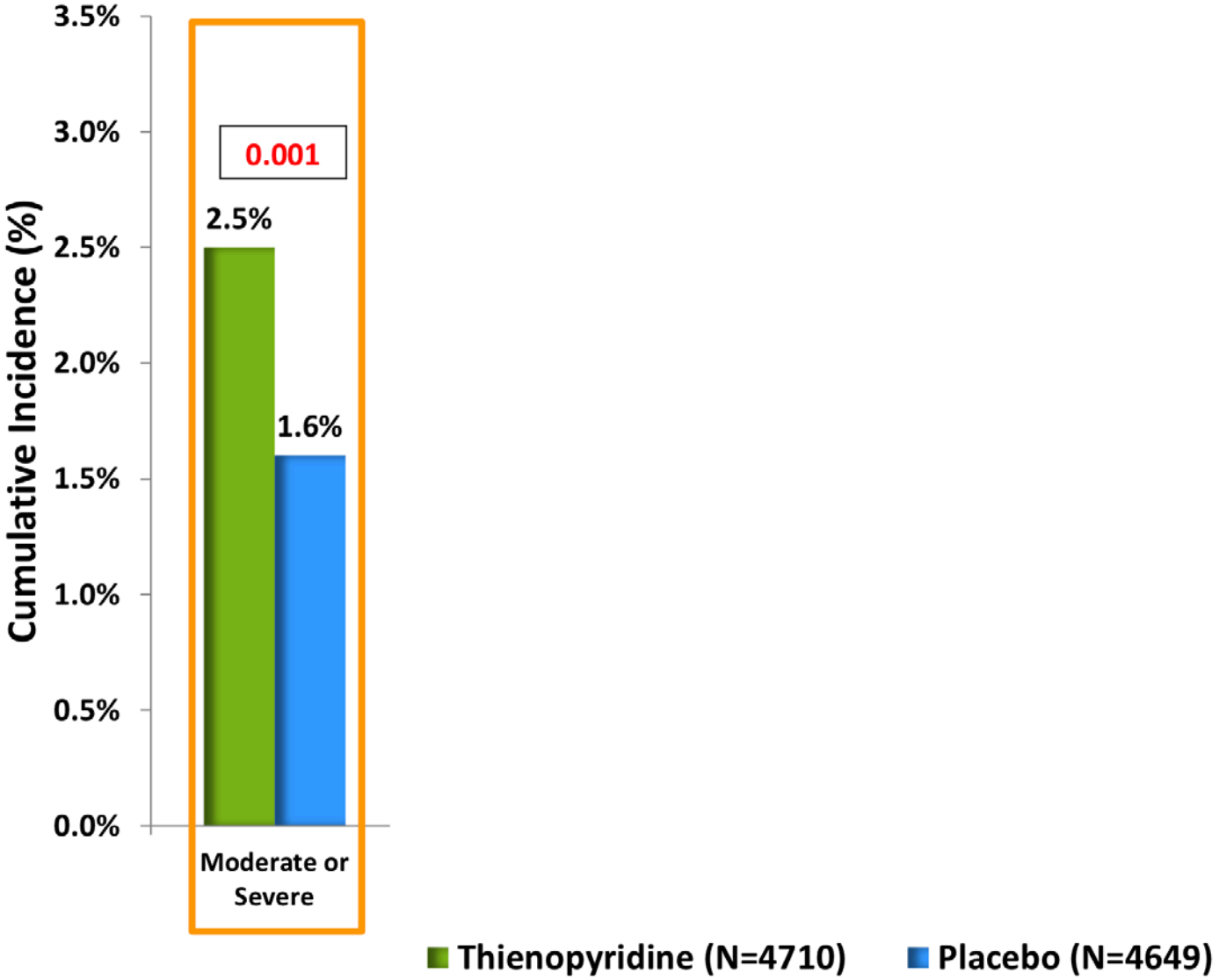
12-30 Months:
HR 0.59 (0.45-0.78)
1.8% vs. 2.9%
P<0.001

# At Risk								
Thienopyridine	5020	4920	4851	4792	4721	4641	4588	3066
Placebo	4941	4820	4751	4686	4607	4547	4491	3052

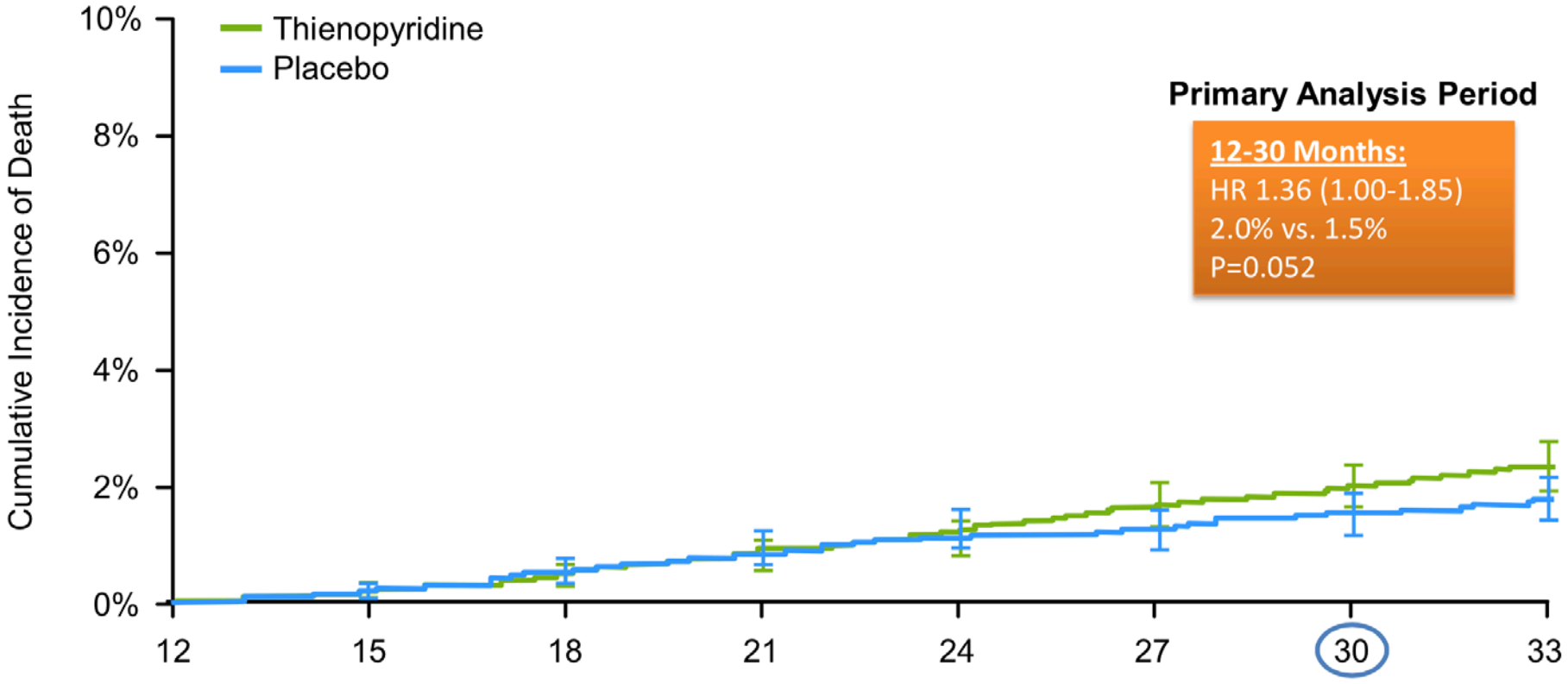
DAPT – wie lange nach Drug-eluting Stent?

- 1-3 Monate
- 6 Monate
- 12 Monate
- 30 Monate

Primary Safety End Point (Moderate or Severe Bleeding): 12-30 Months

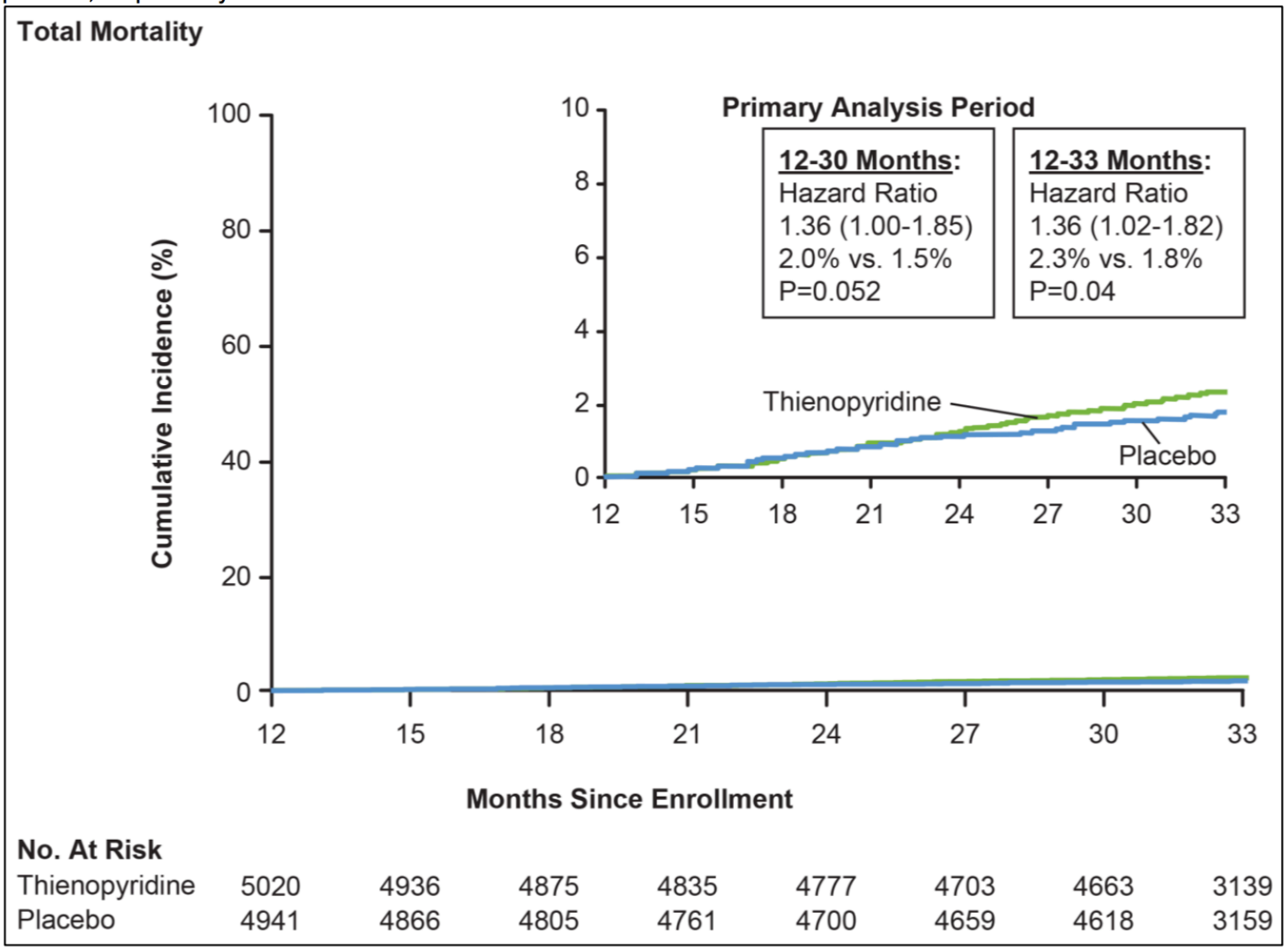


All-Cause Mortality



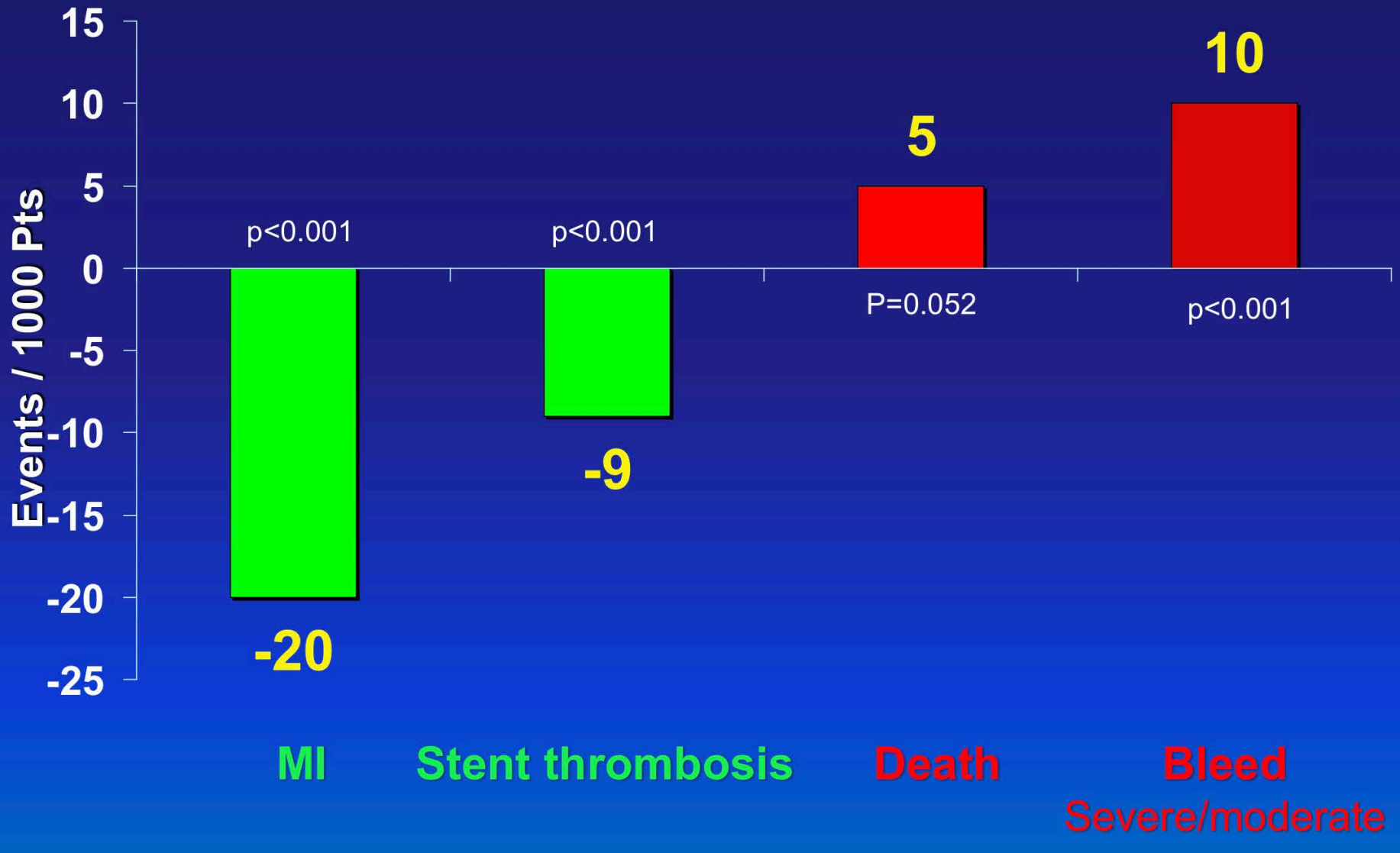
# At Risk								
Thienopyridine	5020	4936	4875	4835	4777	4703	4663	3139
Placebo	4941	4866	4805	4761	4700	4659	4618	3159

Figure S2. Cumulative Incidence of All-Cause Mortality, According to Treatment Group.
Cumulative incidence curve is shown for the effectiveness outcome of myocardial infarction in the intention-to-treat analysis population. Randomization occurred at 12 months after stenting. The primary analysis period was 12-30 months after percutaneous coronary intervention, e.g. the 18 months after randomization over which subjects were treated with study drug. Subjects were followed for an observational period of an addition three months, off study drug and off open label thienopyridine treatment, to a total of 33 months, e.g. 21 months post randomization. P values were calculated with stratified log-rank test. Error bars indicate 95% confidence limits. The number at risk is defined as the number of subjects without the event of interest and available for subsequent follow-up. The number at risk at the start of final 33-month visit (e.g. 20 months post randomization) were 4,465 vs. 4,425 for continued thienopyridine vs. placebo, respectively.



DAPT

For Every 1000 Pts with continued DAPT up to 30 months



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- DAPT = dual antiplatelet therapy
  - Italic
  - ISAR-Safe
  - DAPT

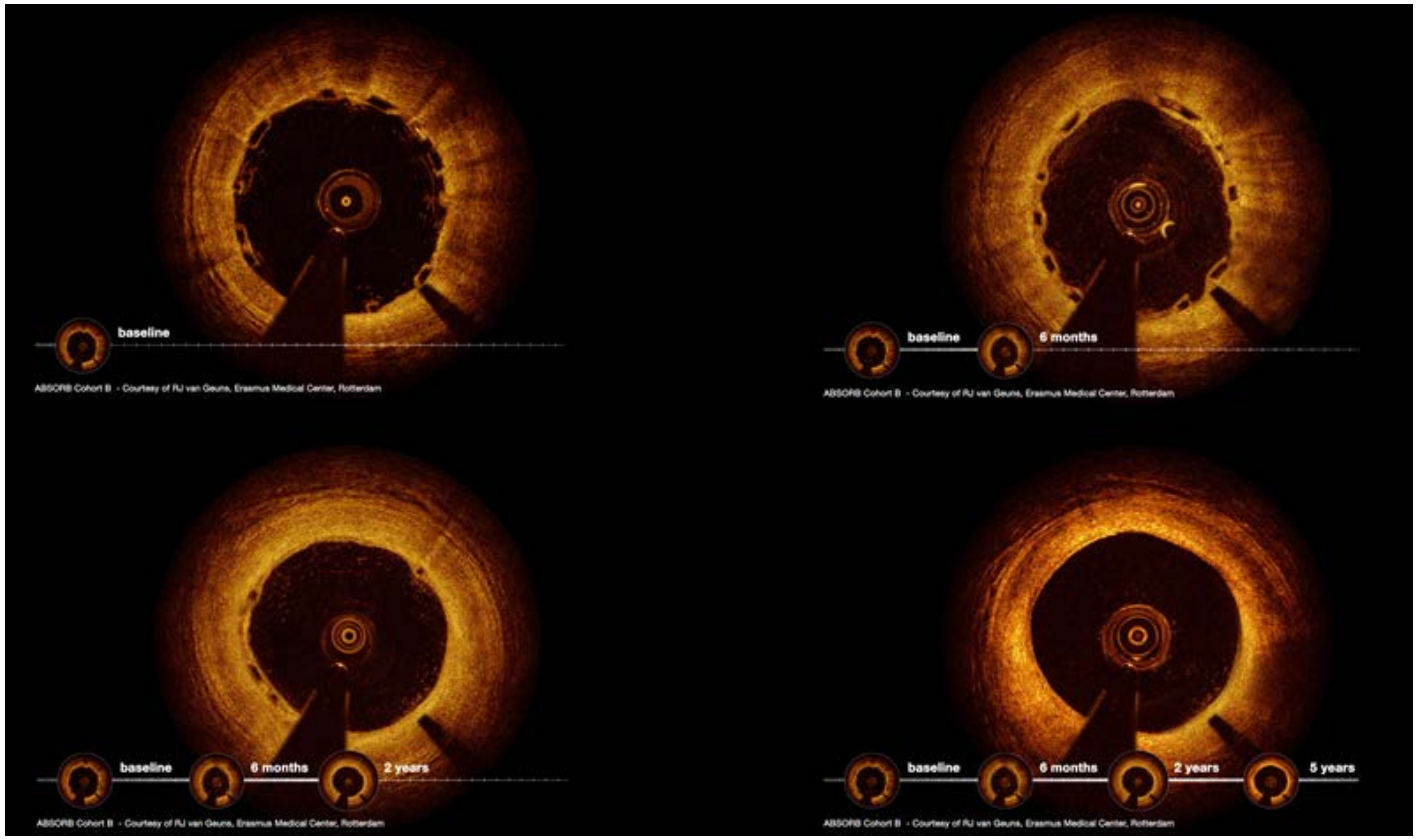
- **Scaffold = bioresorbable “stent”**

Absorb Cohort B – 5 years follow-up

OCT Images Over Time Showing Complete Resorbtion of the Scaffold Struts

Baseline

6 Months



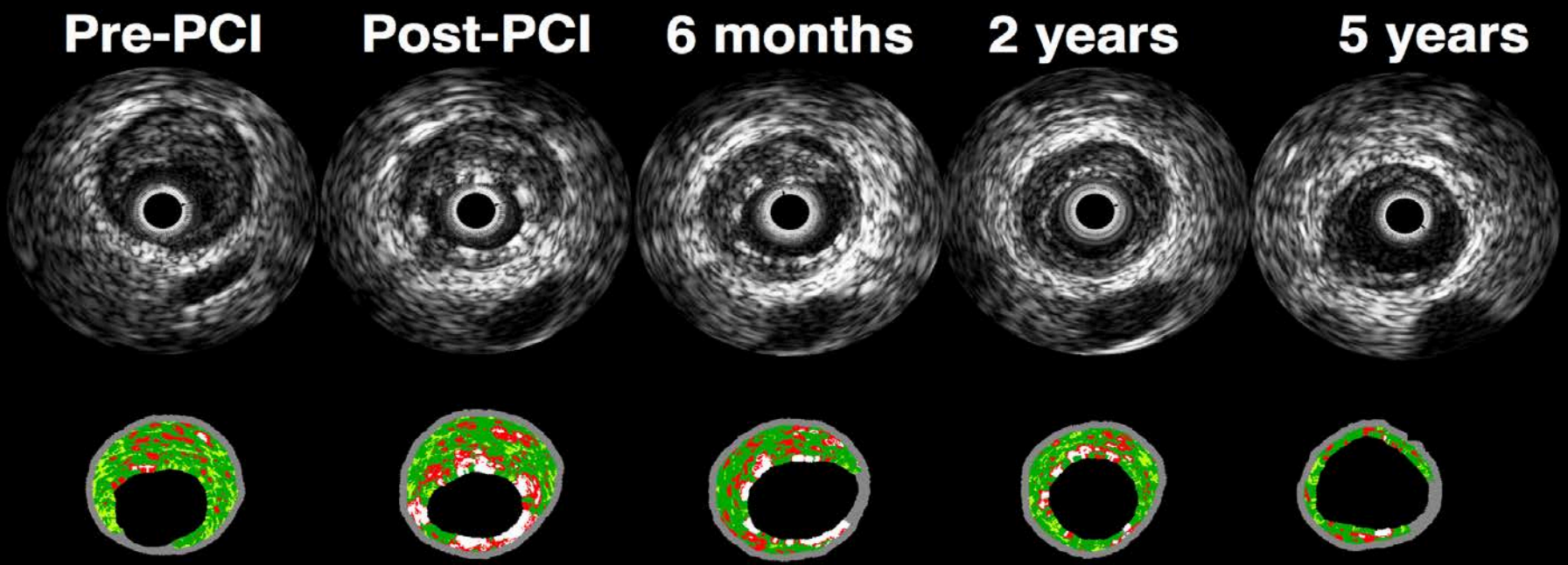
2 Years

5 Years

Courtesy of Dr RJ v Geuns, Rotterdam, The Netherlands

Absorb Cohort B1 5 Year Results; B de Bruyne, TCT 2014

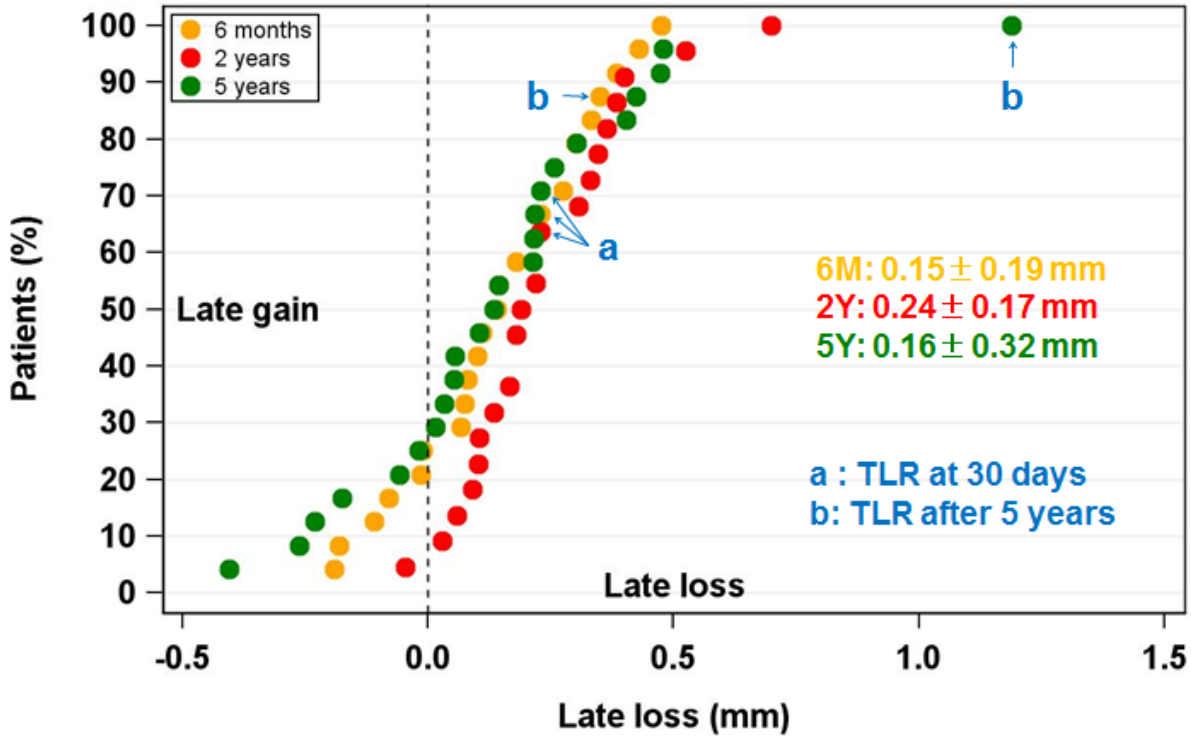
Plaque- und Mediareduktion führt zum Lumenzuwachs



Mean lumen area (mm^2)	6.95	6.17	6.56	8.09
Plaque area (mm^2)	8.78	9.17	7.54	7.07
Vessel area (mm^2)	15.72	15.34	14.09	13.76

ABSORB COHORT B – 5 YEARS

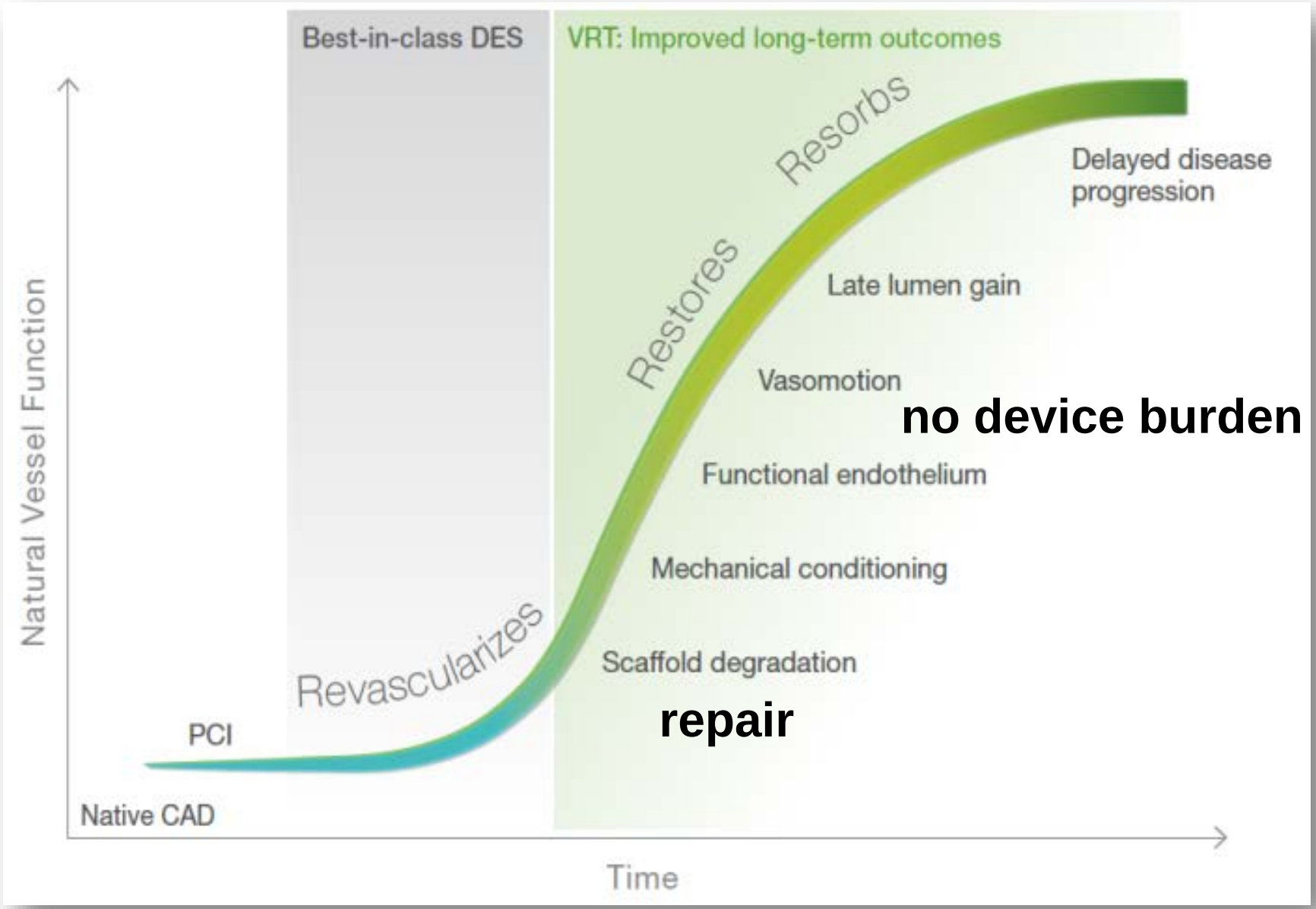
- Summary of Late Loss at 5-years



	6 months n=24	2 years n=22	5 years n=24	Diff 6m vs. 2yrs n=22	Diff 6m vs. 5yrs n=24	Diff 2yrs vs. 5yrs n=22
In scaffold mean late loss	0.15±0.19	0.24±0.17	0.16±0.32	0.10±0.17	0.01±0.29	-0.11±0.18
P-values				0.0133	0.8368	0.0035

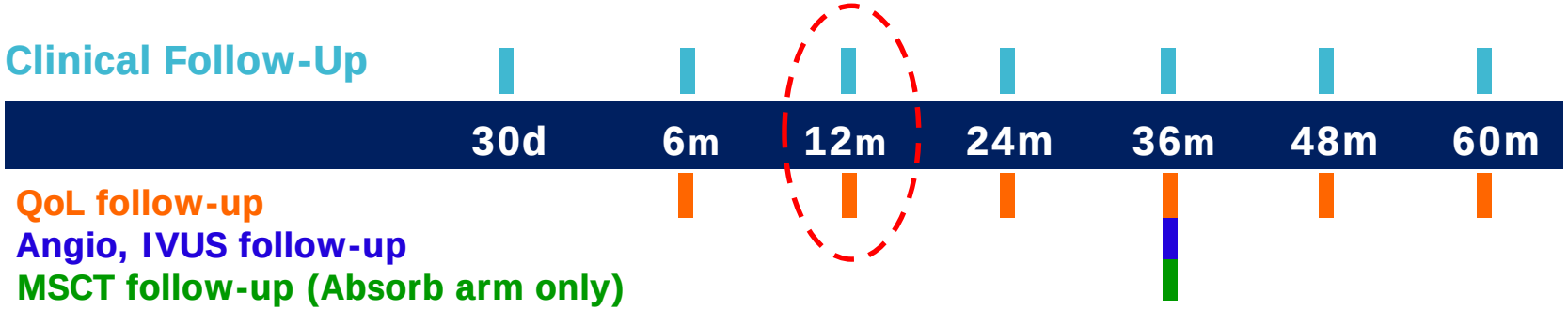
Absorb Cohort B1 5 Year Results; B de Bruyne, TCT 2014

Ziele der Vascular Reparative Therapy (VRT)



ABSORB II Study Design

501 subjects
Randomized 2:1 Absorb BVS:XIENCE / 46 sites (Europe and New Zealand)



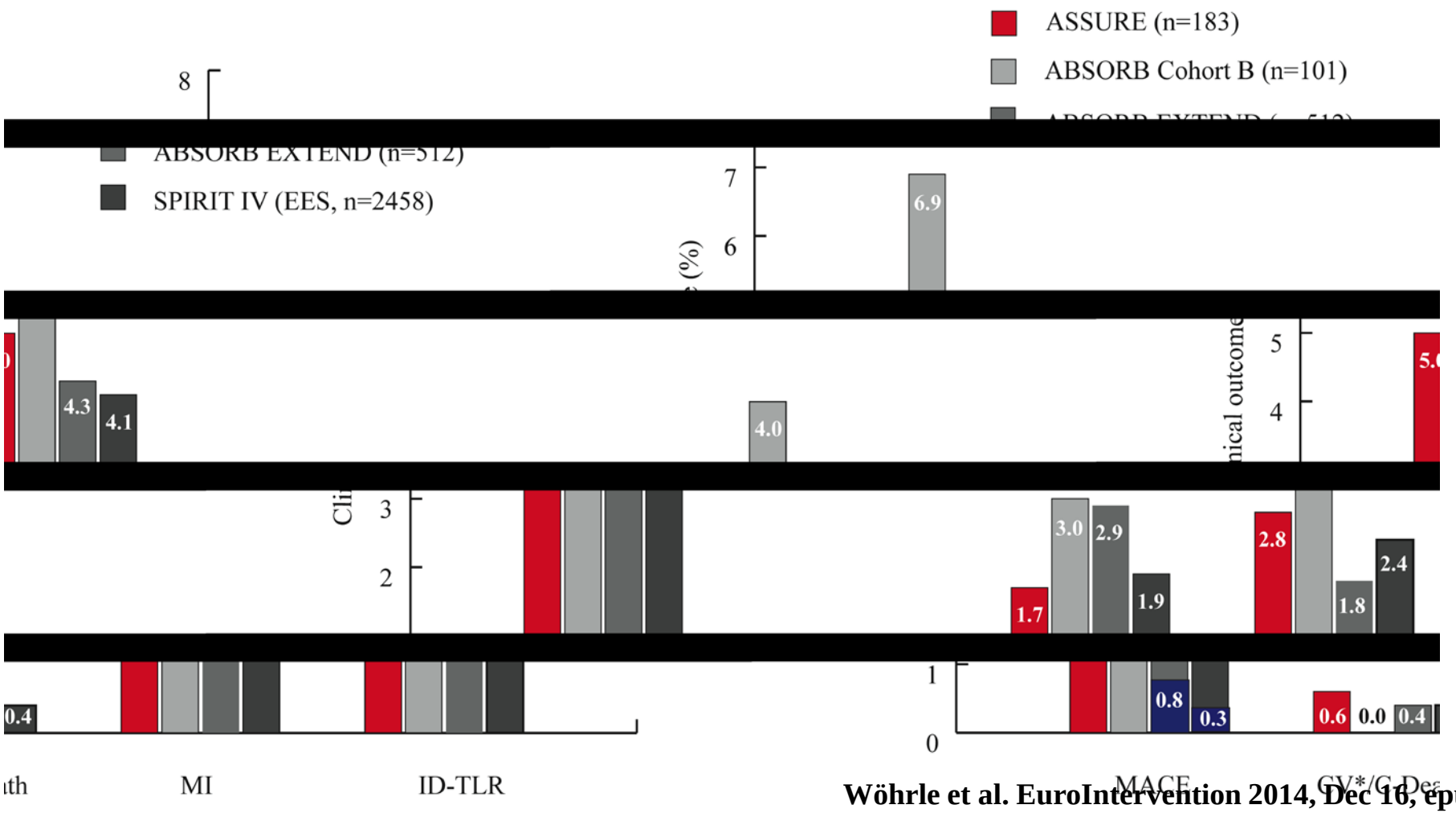
Study Objective	Randomized against XIENCE control. First Patient In: 28-Nov-2011
Co-primary Endpoints	Vasomotion assessed by change in Mean Lumen Diameter between pre- and post-nitrate at 3 years (superiority) Minimum Lumen Diameter (MLD) at 3 years post nitrate minus MLD post procedure post nitrate (non-inferiority, reflex to superiority)
Treatment	Up to 2 *de novo* lesions in different epicardial vessels Planned overlapping allowed in lesions ≤ 48 mm
Device Sizes	Device diameters: 2.5, 3.0, 3.5 mm Device lengths: 12 (3.5 mm diameter only), 18, 28 mm

Clinical Outcomes

Cumulative incidence in percentage	Absorb 335 pts	Xience 166 pts	*p* value
Composite of cardiac death, target vessel MI and clinically indicated target lesion revascularization (TLF, DoCE)	**4.8 %**	**3.0 %**	**0.35**
Cardiac death	0 %	0 %	1.00
Target vessel MI	4.2 %	1.2 %	0.07
Clinically indicated TLR	1.2 %	1.8 %	0.69
All TLR	1.2 %	1.8 %	0.69
Composite of all death, all MI and all revascularization (PoCE)	**7.3 %**	**9.1 %**	**0.47**
All death	0 %	0.6 %	0.33
All MI	4.5 %	1.2 %	0.06
All revascularization	3.6 %	7.3 %	0.08

ASSURE registry
ABSORB postmarketing surveillance registry to monitor the everolimus eluting bioresorbable vascular scaffold in patients with coronary artery disease
ClinicalTrials.gov: NCT01583608

Ulm, Hamburg, Essen, Kiel, Bernau, Coburg



Wöhrle et al. EuroIntervention 2014, Dec 16, epub

The rate of ST in individual populations *

Study (Journal / international congress)	Population	Follow up	Total, N	Acute ST in total, N (%)	Subacute ST in total, N (%)	Early ST in total, N (%)	ST in total, N (%)	SAP, N	ST in SAP, N (%)	ACS, N	ST in ACS, N (%)	STEMI, N	ST in STEMI, N (%)
Kraak et al., AMC Single Centre (EIJ)	All-comers	6M	135	0(0%)	3 (2.2%)	3 (2.2%)	4 (3.0%)	82	1 (1.2%)	53	3 (5.7%)	17	0 (0%)
ABSORB FIRST (euroPCR2014)	All-comers	1M	800	0(0%)	2 (0.3%)	2 (0.3%)	2 (0.3%)	295	N/A	505	N/A	N/A	N/A
Azzalini et al. (euroPCR2014)	All-comers	N/A	339	0 (0%)	4 (1.2%)	4 (1.2%)	4 (1.2%)	N/A	3 (N/A)	N/A	0 (N/A)	N/A	1 (N/A)
Abizaid et al, ABSORB EXTEND (EIJ)	SAP	12M	512	0 (0%)	2 (0.4%)	2 (0.4%)	4 (0.8%)	512	4 (0.8%)	-	-	-	-
Serruys et al., ABSORB B (EIJ)	SAP	36M	101	0 (0%)	0 (0%)	0 (0%)	0 (0%)	101	0 (0%)	-	-	-	-
Onuma et al., ABSORB A (JACC int.)	SAP	60M	30	0 (0%)	0 (0%)	0 (0%)	0 (0%)	30	0 (0%)	-	-	-	-
CORONARY CTO(euroPCR2014)	SAP	6M	35	0 (0%)	0 (0%)	0 (0%)	0 (0%)	35	0 (0%)	-	-	-	-
Serruys et al., ABSORB II (Lancet in press)	SAP / UAP	12M	335	1 (0.3)	1 (0.3)	2 (0.6)	3 (0.9%)	267	3 (1.1%)	68	0 (0%)	-	-
ASSURE registry (euroPCR2014)	SAP / UAP	12M	183	0 (0%)	0 (0%)	0 (0%)	0 (0%)	144	0 (0%)	39	0 (0%)	-	-
BVS EXPAND (euroPCR2014)	SAP / UAP	6M	200	0 (0%)	0 (0%)	0 (0%)	4 (2.2%)	N/A	N/A	N/A	N/A	-	-
Gori et al (EIJ)	ACS	1M	150	1 (0.7%)	1 (0.7%)	2 (1.4%)	4 (2.7%)	-	-	150	4 (2.7%)	66	N/A
POLAR ACS (euroPCR2014)	ACS	12M	100	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	100	0 (0%)	16	0 (0%)
Kajiya et al. (EIJ)	STEMI	3M	11	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	-	-	11	0 (0%)
Diletti et al. , BVS STEMI (EHJ)	STEMI	1M	49	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	-	-	49	0 (0%)
Kocka et al., PRAGUE-19 (EHJ)	STEMI	4M	41	0 (0%)	1 (2.4%)	1 (2.4%)	1 (2.4%)	-	-	-	-	41	1 (2.4%)
Wiebe et al. (Clin Res Cardiol)	STEMI	6M	25	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-	-	-	-	25	0(0%)
Ielasi et al., RAI registry (EIJ in press)	STEMI	6M	74	0(0%)	1(1.4%)	1(1.4%)	1(1.4%)	-	-	-	-	74	1(1.4%)
Weighted average excluding the GHOST-EU registry	**Average F/U: 10.6 Months**		**3120**	**0.06%**	**0.48%**	**0.54%**	**0.89%**	**1171**	**0.68%**	**410**	**1.71%**	**299**	**0.67%**
Capodanno et al., GHOST (EIJ)	All-comer	6M	1189	5 (0.4%)	11 (0.9%)	16 (1.3%)	23 (2.1%)	626	9 (1.4%)	563	14 (2.5%)	192	4 (2.1%)
Weighted average including the GHOST-EU registry	**Average F/U: 10.3 Months**		**4309**	**0.16%**	**0.60%**	**0.76%**	**1.22%**	**1797**	**0.94%**	**973**	**2.16%**	**491**	**1.22%**

*** ST= scaffold thrombosis, SAP= stable/silent angina pectoris, ACS=acute coronary syndrome, STEMI=ST-segment elevation myocardial infarction**

A Randomized Comparison of Combined Ticlopidine and Aspirin Therapy Versus Aspirin Therapy Alone After Successful Intravascular Ultrasound–Guided Stent Implantation

Intravascular ultrasound guided stenting
226 patients

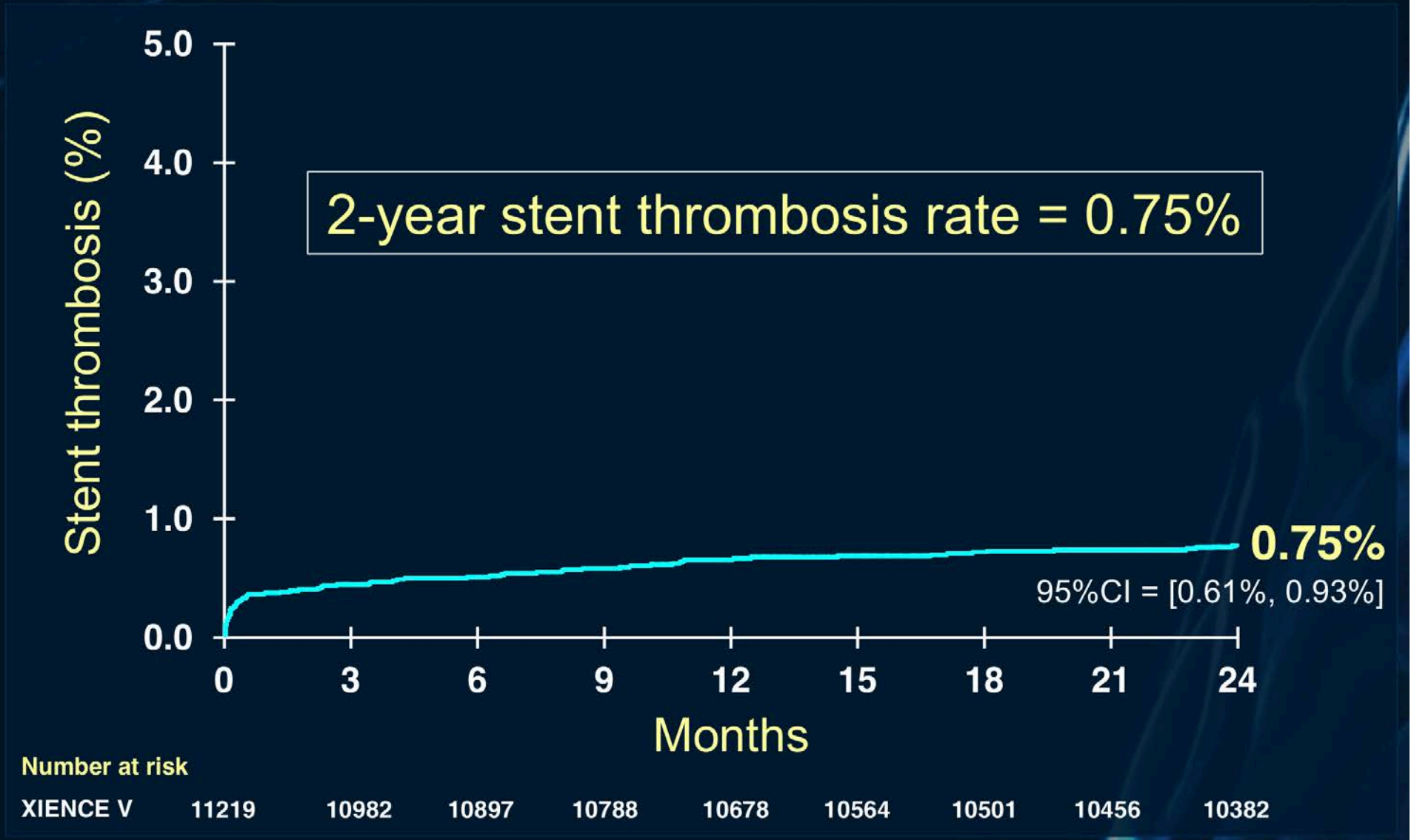
Stent thrombosis at 1 month	2.9% versus 0.8% (p=0.20)
MACE	3.9% versus 0.8% (p=0.10)

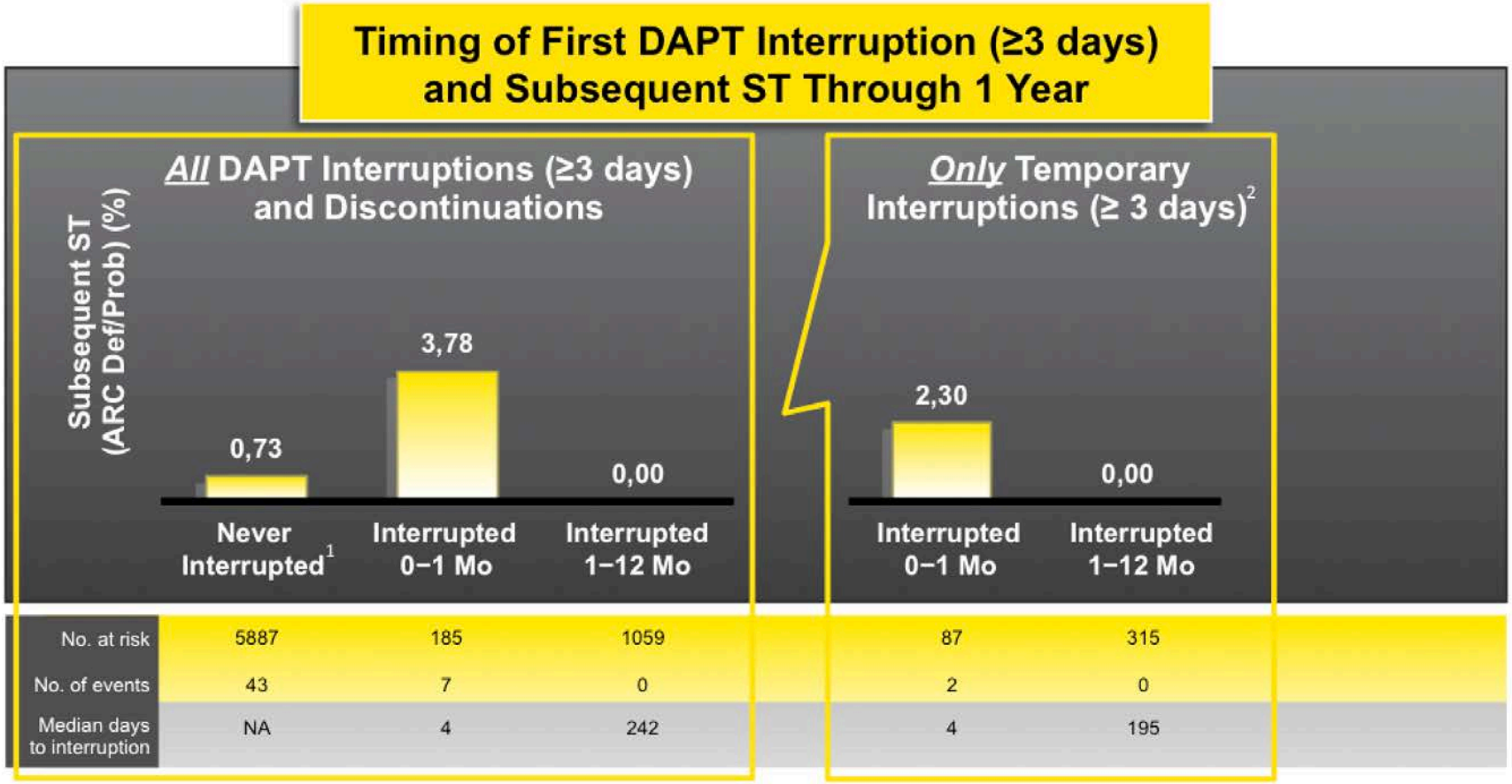
MACE = stent thrombosis, death, MI, need for revascularization, significiant medication side effects

Circulation 1996; 93:215-222
Colombo A

Stent Thrombosis Through 2 Years

N = 11,219 Xience V pts





Eur Heart J 2014

Stent Thrombosis According to the Timing of Permanent DAPT Interruption*

Stent thrombosis through the entire 2-year follow-up period:	ST, % No DAPT interruption except possibly after ST	ST, % Permanent DAPT discontinuation in this interval*	HR [95% CI]	P Value
Between 0 and 1 mos	0.83% (58) (N at risk = 7,152)	4.95% (11) (N at risk = 229)	6.13 [3.22, 11.68]	<0.0001
Between 1 and 3 mos	0.83% (58) (N at risk = 7,152)	2.78% (2) (N at risk = 76)	3.38 [0.82, 13.82]	0.07
Between 3 and 6 mos	0.83% (58) (N at risk = 7,152)	0.78% (1) (N at risk = 146)	0.85 [0.12, 6.13]	0.87
Between 6 and 12 mos	0.83% (58) (N at risk = 7,152)	0.45% (4) (N at risk = 934)	0.52 [0.19, 1.43]	0.20
Between 12 and 24 mos	0.83% (58) (N at risk = 7,152)	0.16% (3) (N at risk = 1,925)	0.19 [0.06, 0.60]	0.002
Between 0 and 24 mos	0.83% (58) (N at risk = 7,152)	0.64% (21) (N at risk = 3,310)	0.77 [0.47, 1.27]	0.30

Rates are Kaplan-Meier estimates. * Or until the time of a stent thrombosis.

Stone TCT

- **DAPT**
  - DAPT nach elektiver DES Implantation: 6 Monate
  - Längere Therapie ist mit mehr Blutungen, einer höheren Mortalität, weniger Stentthrombosen und Myokardinfarkte assoziiert (DAPT)
  - ISAR-SAFE: kein Unterschied (Blutungen verdoppelt)
  - Eine längere (auch kürzere !) DAPT ist eine individuelle Entscheidung
  - Kein DAPT Unterschied zwischen DES und Scaffold