6. Thromboseforum
Stuttgart 30.01.2016

Koronare Herzerkrankung und Klappenerkrankung

Antithrombozytäre Therapie nach Drug-eluting stents (DES) und bioresorbierbaren Scaffolds (BVS) bei stabiler koronarer Herzkrankheit

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Bare-Metal-Stent

Reduktion der subakuten Stentthomboserate (30-Tage) von

-> 25% (ASS Monotherapie) auf

-> 5-7% (Marcumar+ASS) auf

-> unter 3% (ASS+Ticlopidine), STARS, FANTASTIC)

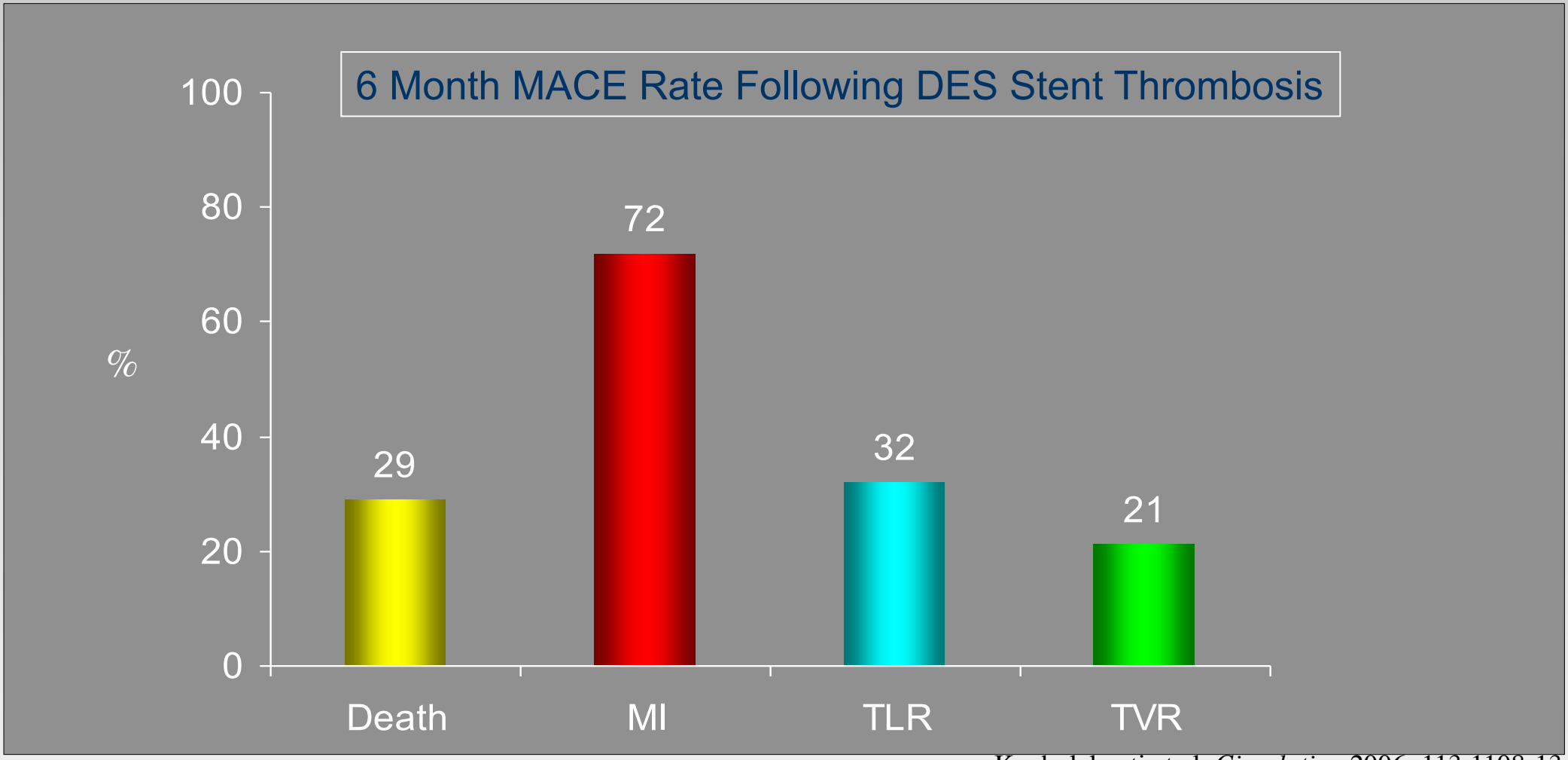
+Hochdruckimplantaion 10-25 bar+Oversizing (IVUS)

<u>Nachteil</u>: Restenoserate von 15-30% !!

Stent Thrombose Outcome

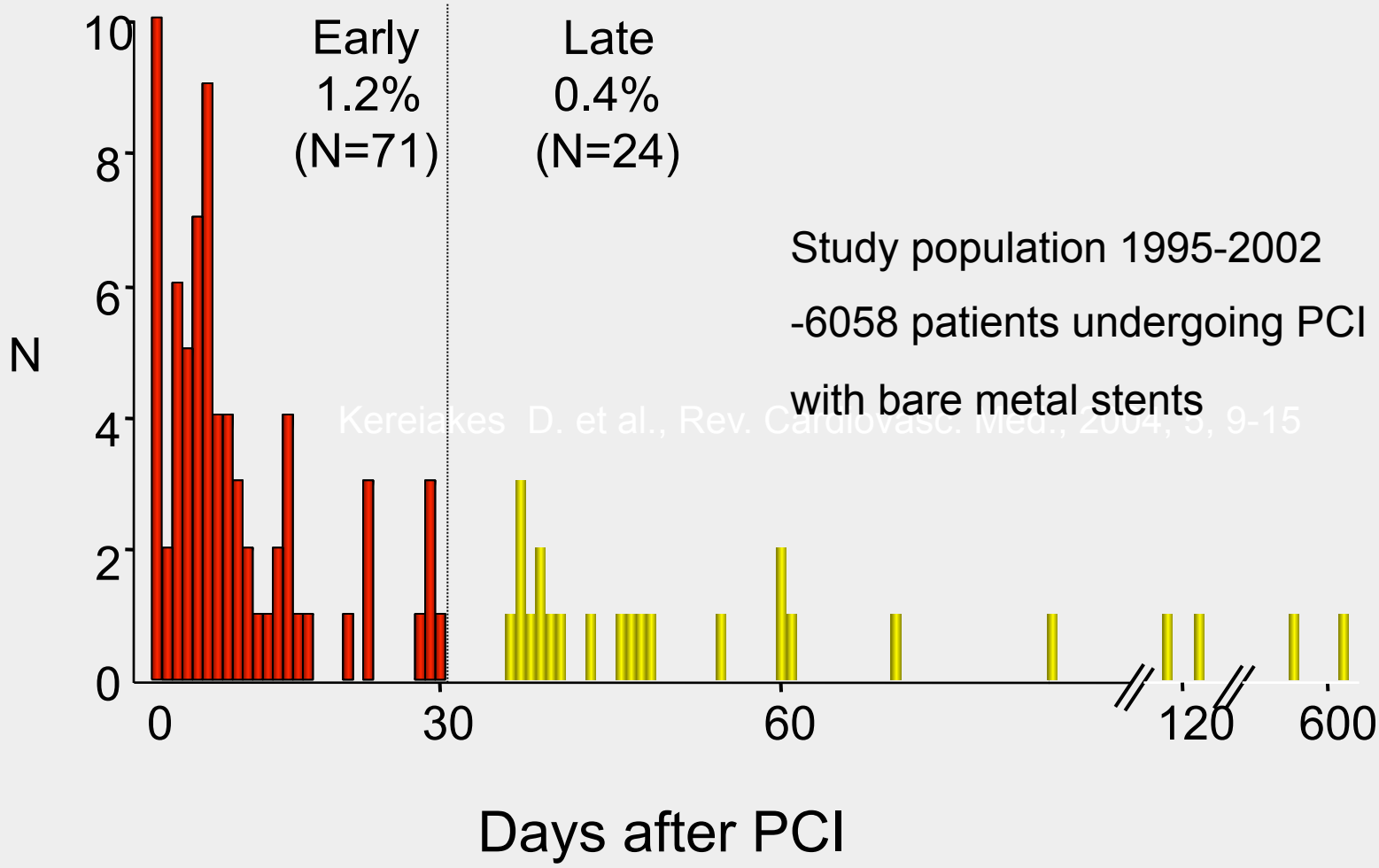
Study population (April 2003-November 2004): 2974 patients treated with DES

Overall incidence of ST: 38/2974 patients (1.3%)



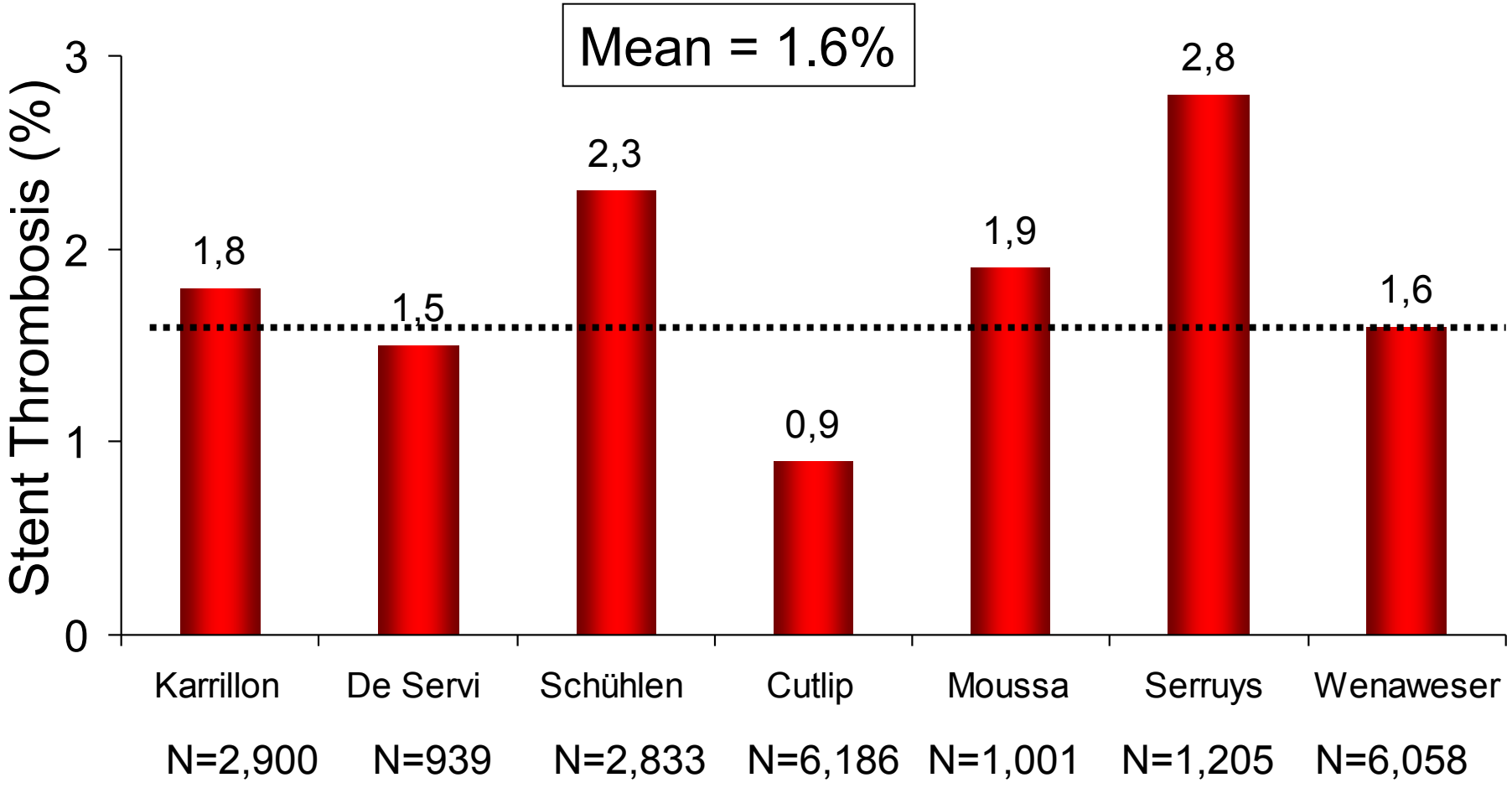
Kuchulakanti et al. *Circulation* 2006; 113:1108-13

Stent Thrombosis
Bare Metal Stents



Wenaweser P et al. *Eur Heart J* 2005;26:1180-7

Akute/Subakute Stenttrhombose
BMS (30 Tage)

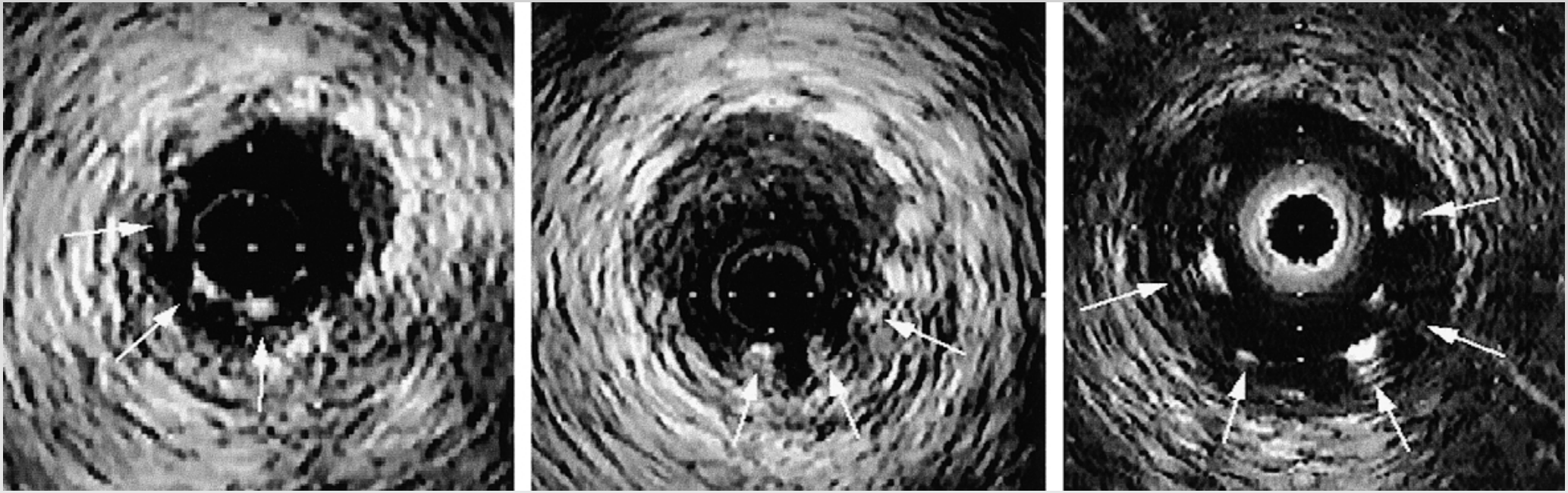


N=21,122

Kereiakes D. et al., Rev. Cardiovasc. Med., 2004, 5, 9-15

Predictors and Outcomes of Stent Thrombosis (POST)

Malapposition



Mild | Moderate | Severe

Uren N.G. et al., European Heart Journal 2002, 23: 124-132

Predictors and Outcomes of Stent Thrombosis (POST)

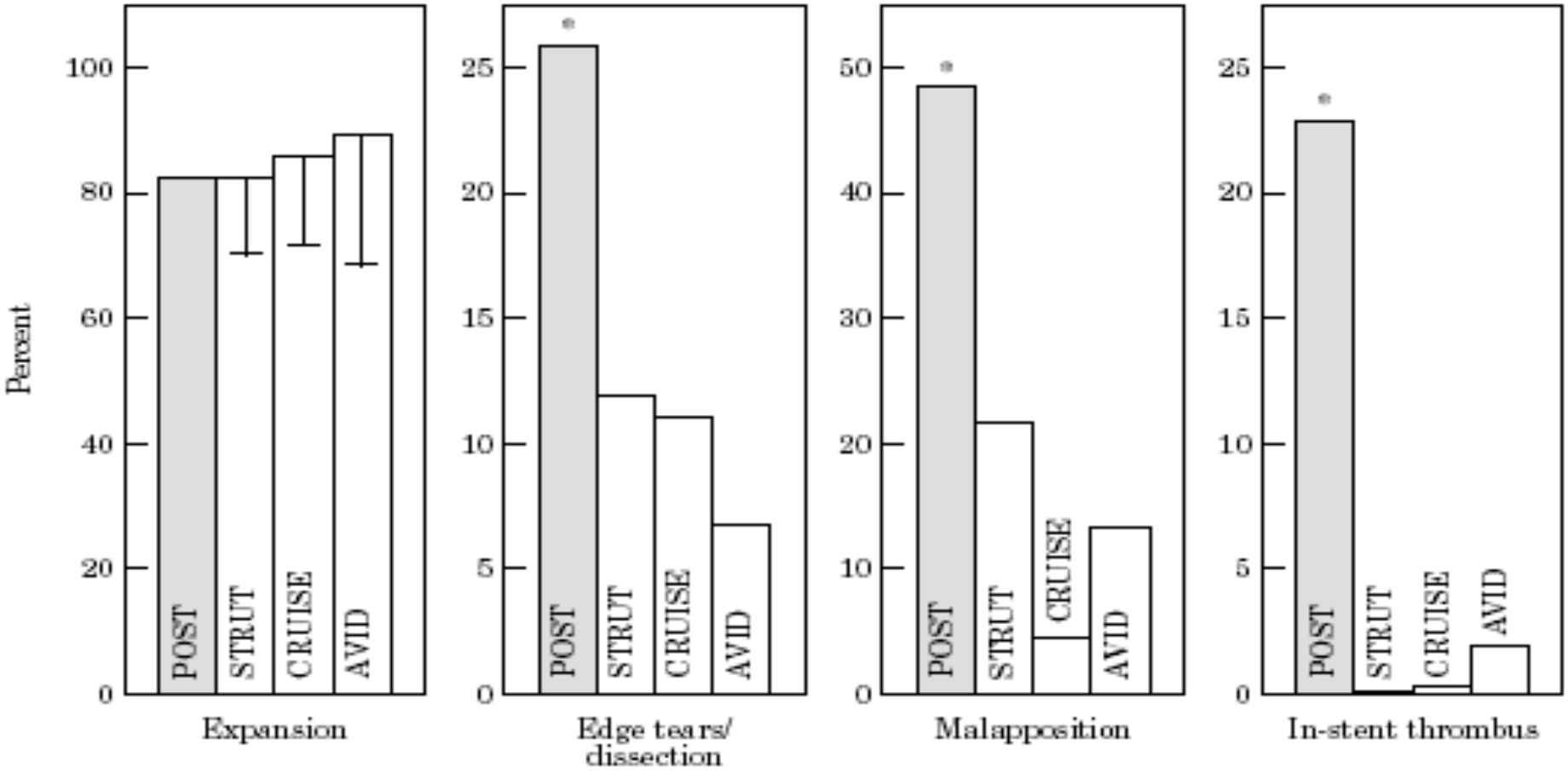
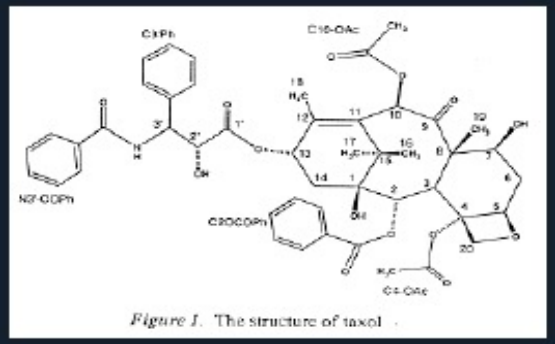
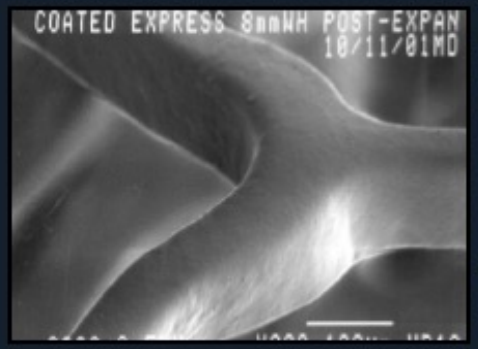
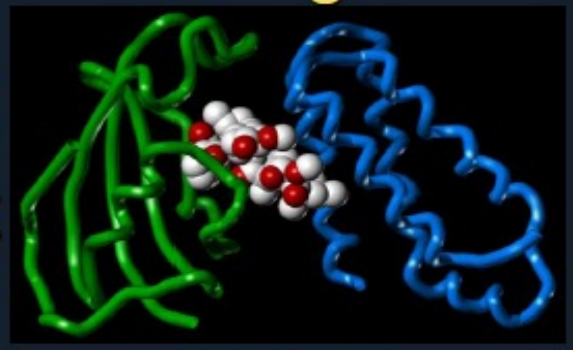
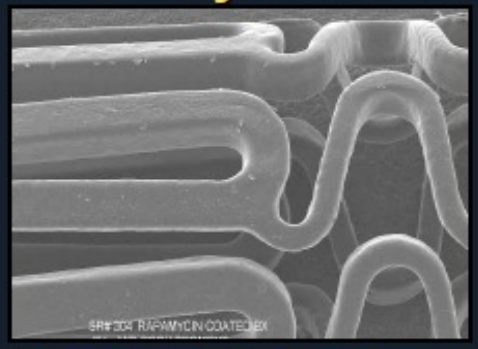


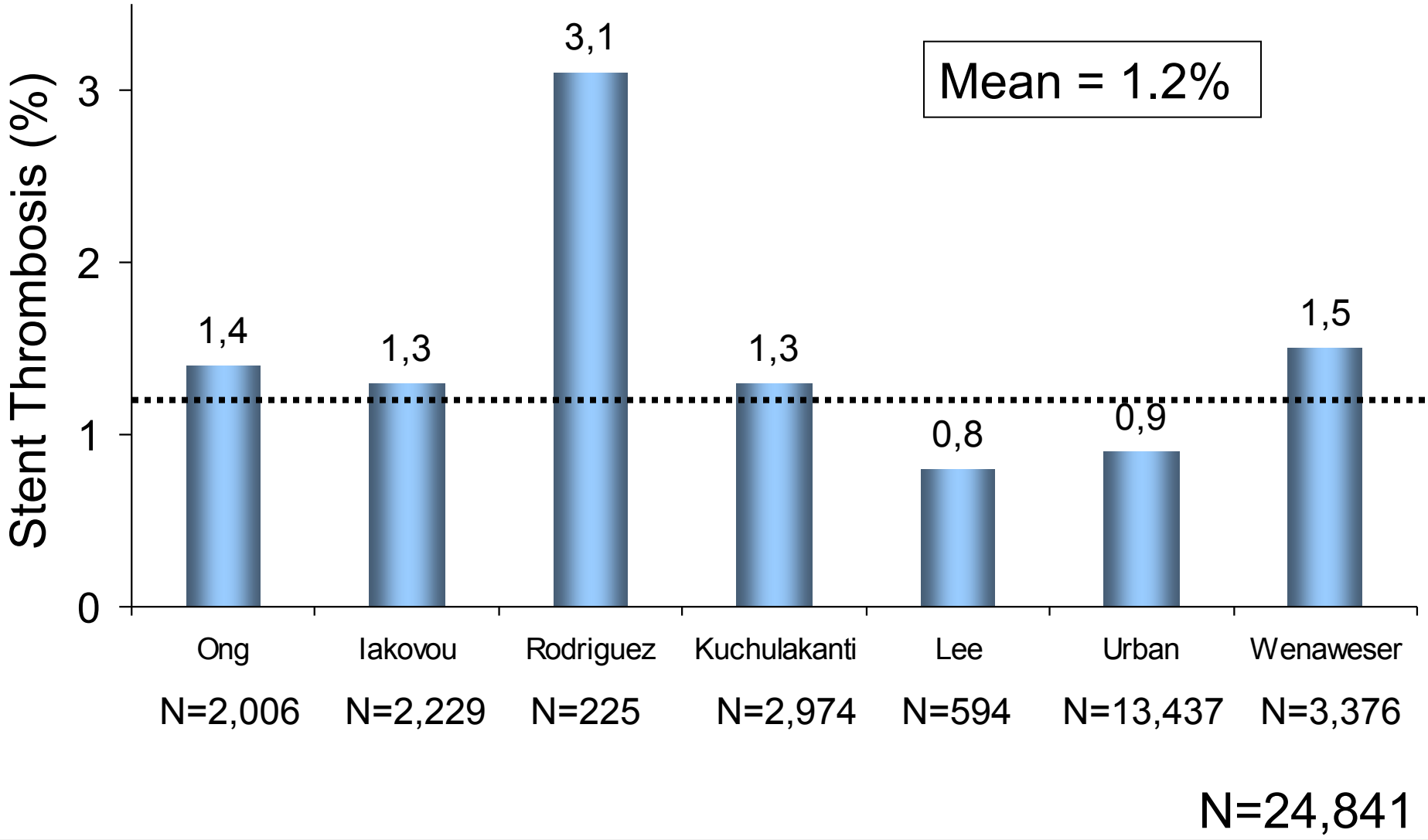
Figure 4 **A direct comparison of POST with existing ultrasound-guided stent deployment registries (STRUT) and ultrasound-guided stent deployment studies (CRUISE, AVID) with respect to percent stent expansion, edge tear/dissection, malapposition, and thrombus (*$P<0{\cdot}05$ vs STRUT, CRUISE, and AVID).**

Drug-eluting stents (DES)

1.Generation, Aufbau

	Drug	Polymer	Stent
TAXUS	 Paclitaxel	 Polyolefin derivative	 Liberté
Cypher	 Sirolimus	 PEVA + PBMA blend	 BX Velocity

Akute/Subakute Stenttrhombose
DES (30 Tage)



Stentthrombose

Frühe ≤ 1 Mo	Späte > 1 Mo ≤ 1Jahr	Sehr späte > 1Jahr

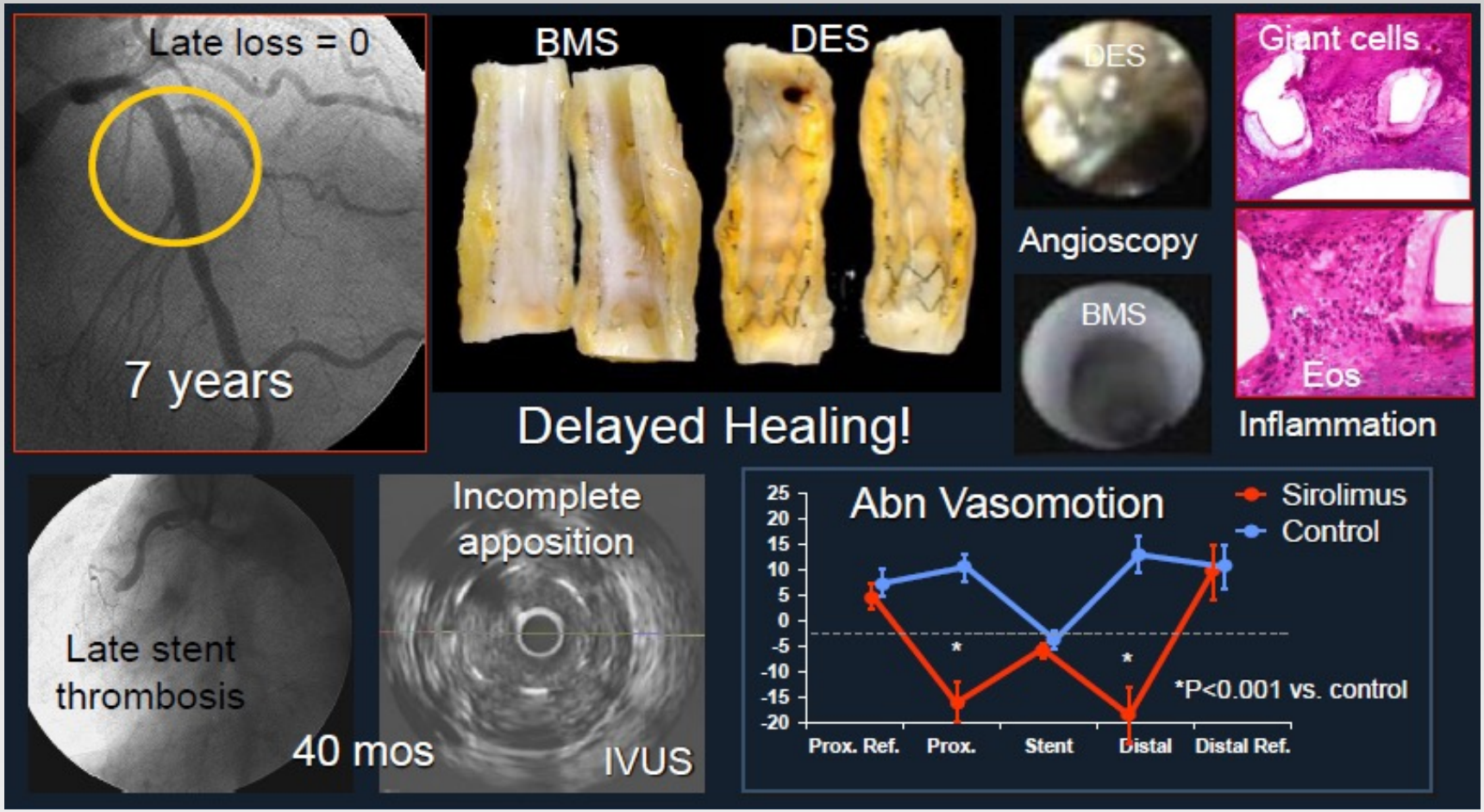
Tag 0	**bis Tag 1**	**Akute Stentthrombose**
>Tag 1	**bis 1 Monat**	**Subakute Stentthrombose (SAT)**
>1 Monat	**to 1 Jahr**	**Späte Stentthrombose (LST)**
(VLST)	**> 1 year**	**Sehr späte Stentthrombose (VLST)**

Empfehlung-> DAPT 12 Monate

Drug-eluting stents (DES)

1.Generation, Limitationen

Durch verzögerte Endotelialisierung Auftreten später Stentthrombosen !!



-> duale Plättchenhemmung (ASS+Clopidogrel) für 6-12 Monate

Stentthrombose

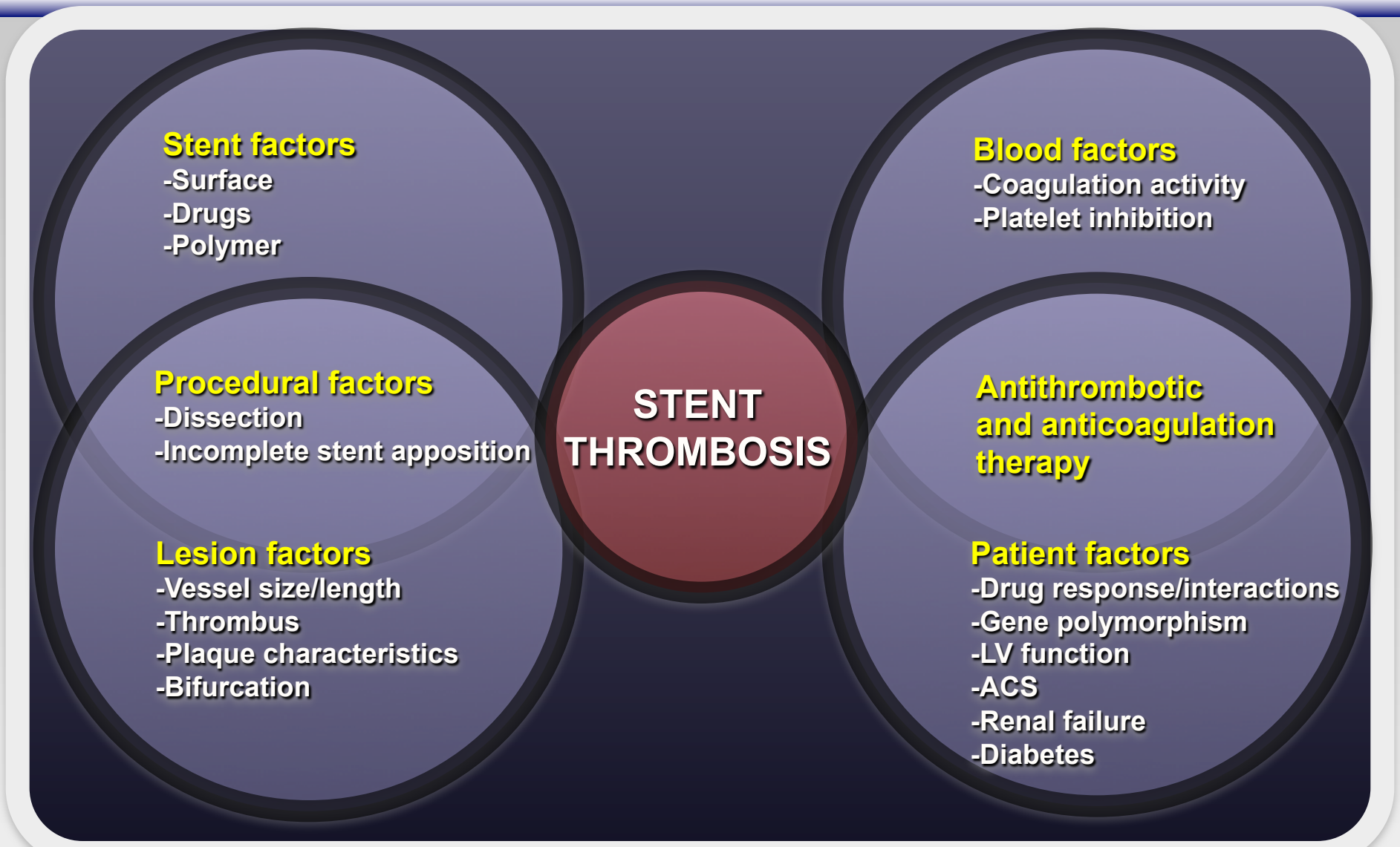
Limitationen

- Herzchirurgischer Standpunkt

Was ist das für eine Behandlung, die das Überleben des Patienten von der täglichen korrekten Einnahme von zwei Tabletten über ein Jahr abhängig macht ??

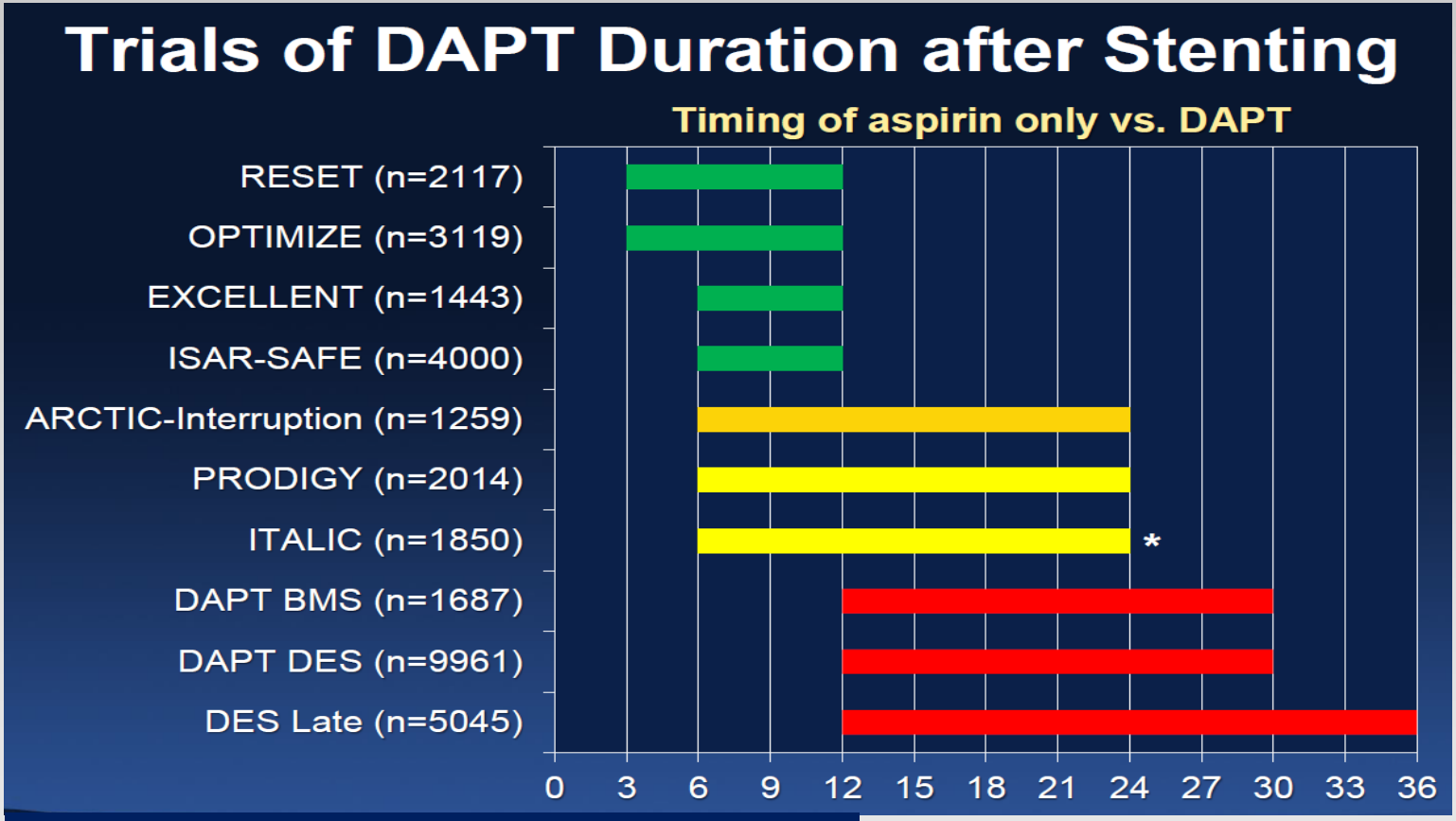
Drug-eluting stents (DES)

Verhinderung der Stentthrombose



Duale Plättchenhemmung-wie lange ?

Meta-Analyse 10 RCTs (31.666 Pat.)



Palmerini et al. Lanect 2015

Duale Plättchenhemmung-wie lange ?

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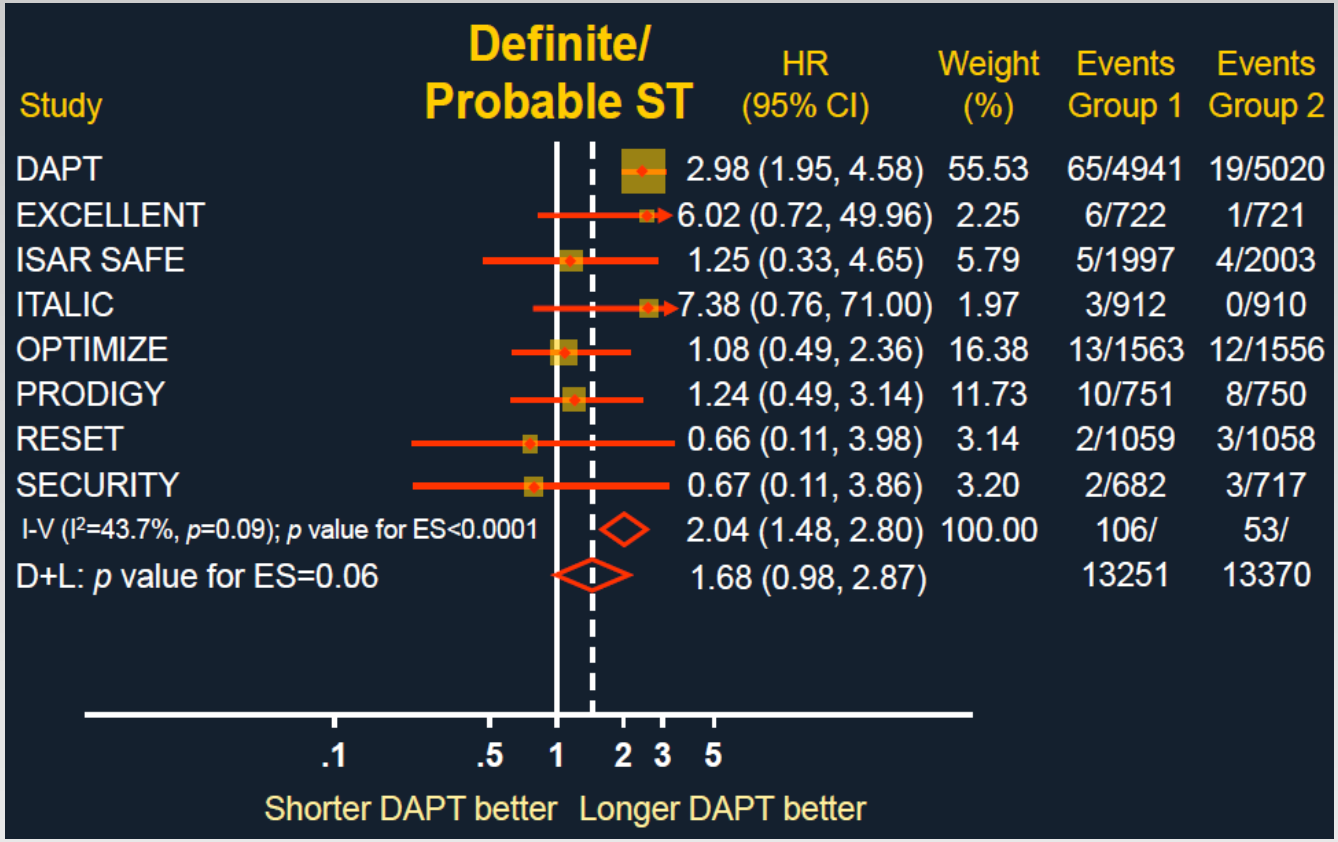
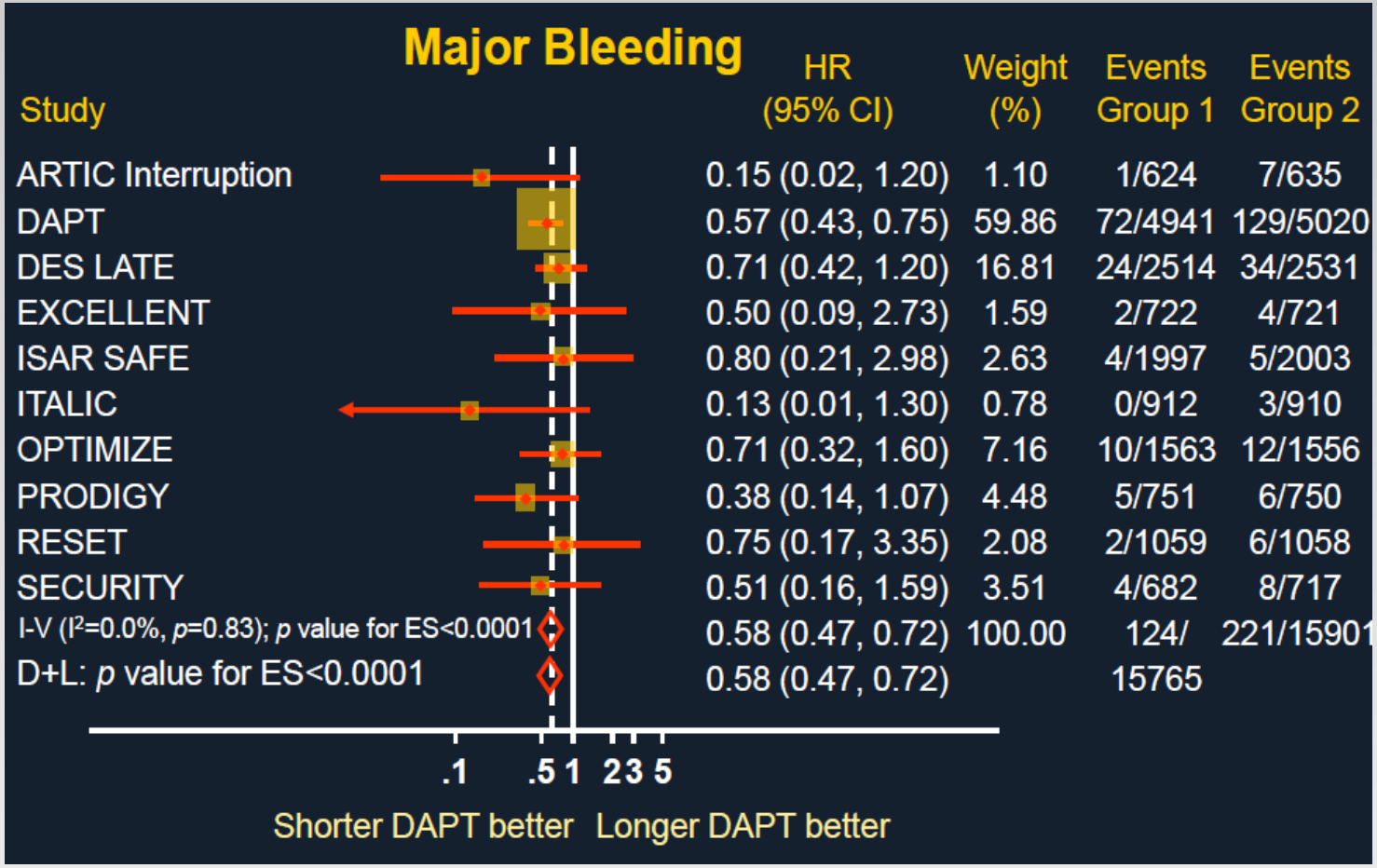


41% ↓ stent thrombosis with prolonged DAPT (p=0.06)

Palmerini et al. Lanect 2015

Duale Plättchenhemmung-wie lange ?

Meta-Analyse 10 RCTs (31.666 Pat.)

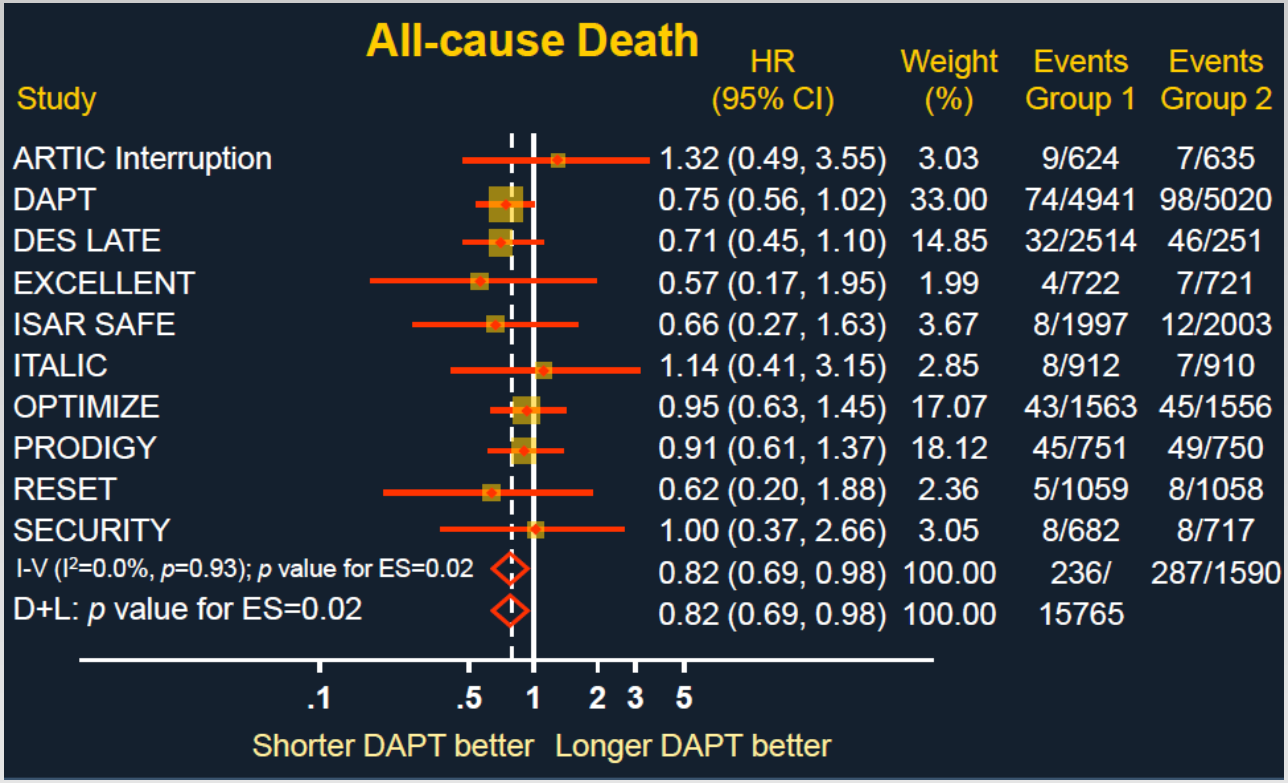


72% ↑ bleeding with prolonged DAPT (p<0.0001)

Palmerini et al. Lanect 2015

Duale Plättchenhemmung-wie lange ?

Meta-Analyse 10 RCTs (31.666 Pat.)

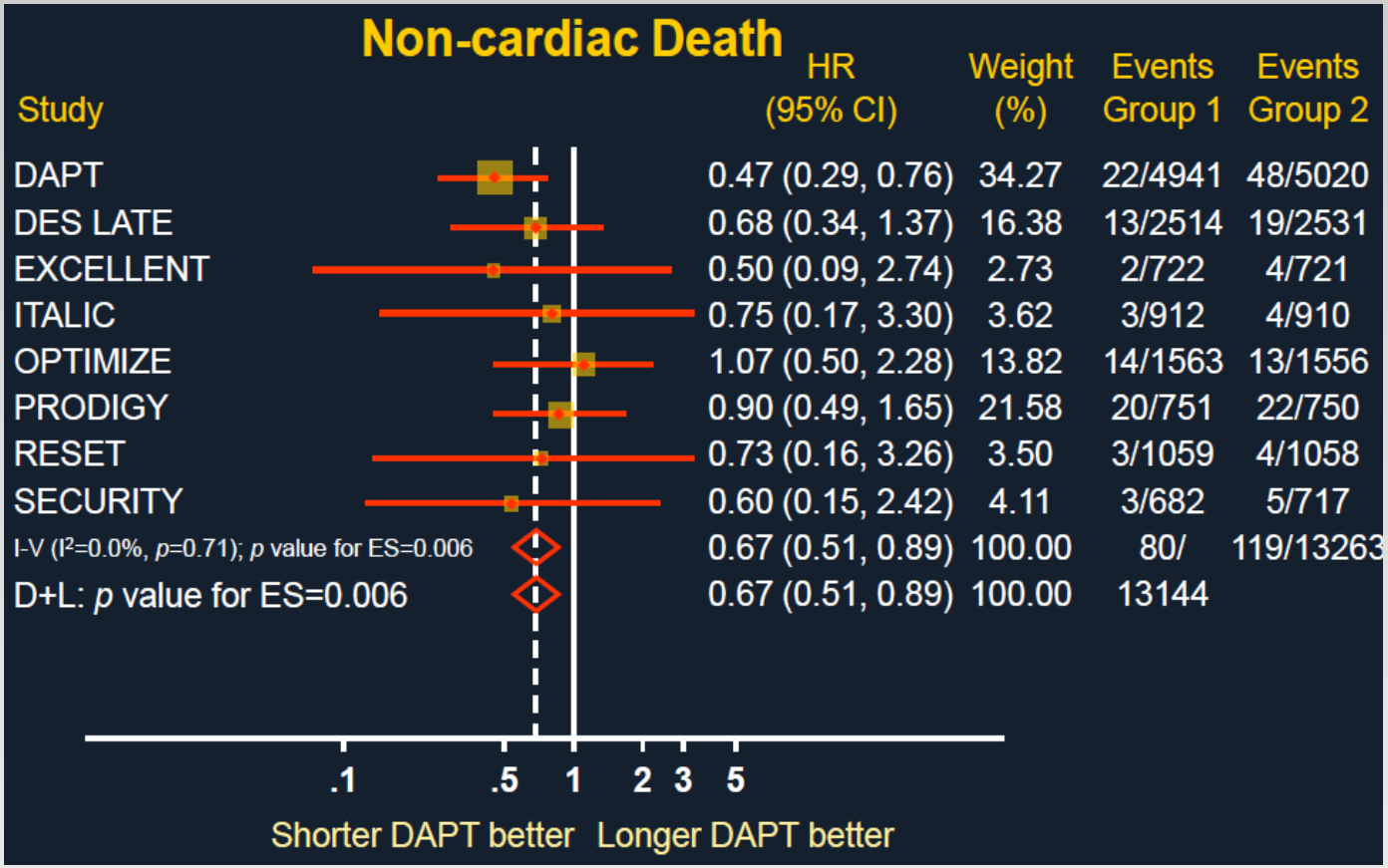


22% ↑ mortality with prolonged DAPT (p=0.02)

Palmerini et al. Lanect 2015

Duale Plättchenhemmung-wie lange ?

Meta-Analyse 10 RCTs (31.666 Pat.)

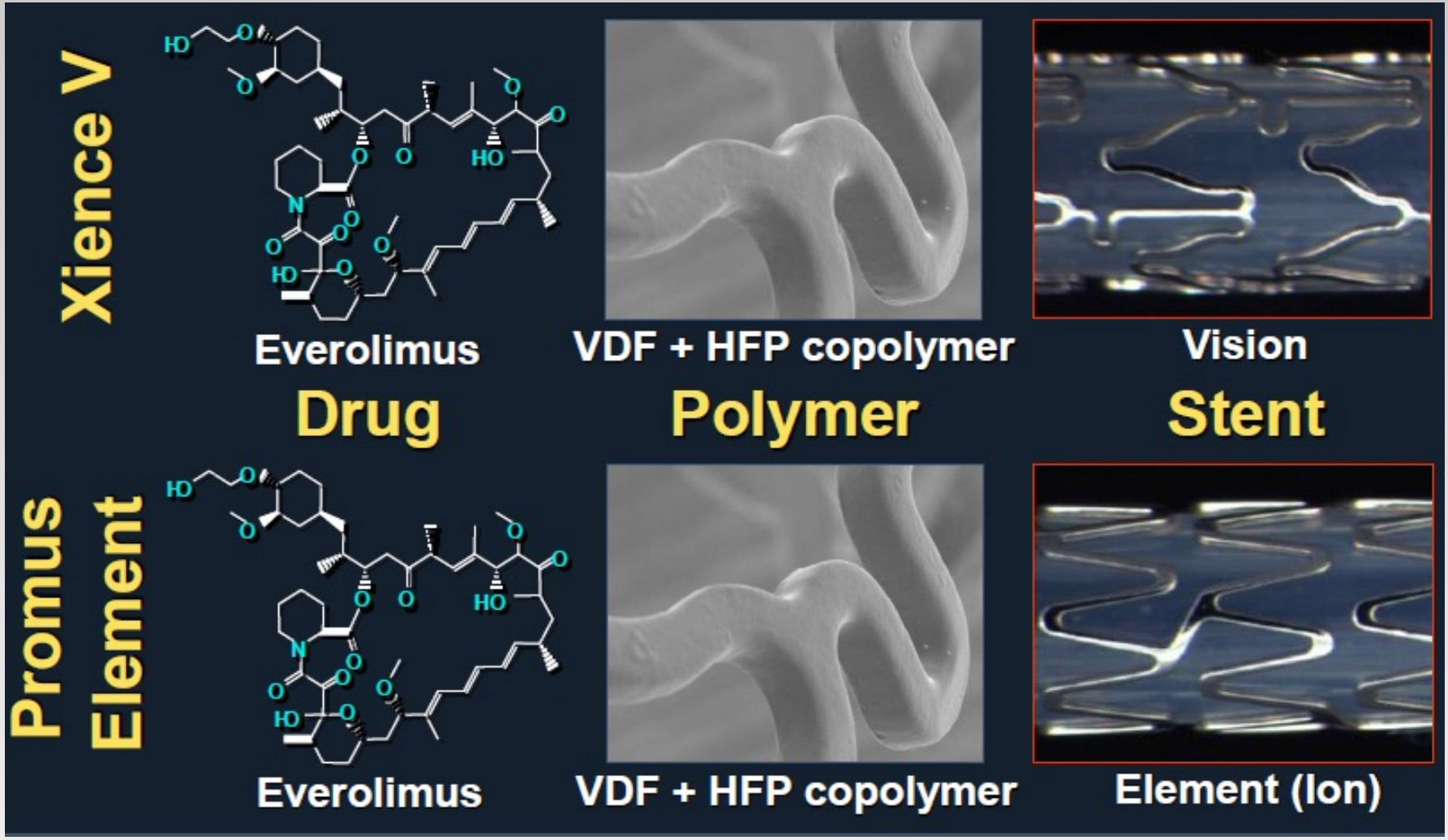


49% ↑ Non-cardiac mortality with prolonged DAPT (p=0.006)

Palmerini et al. Lanect 2015

Drug-eluting stents (DES)

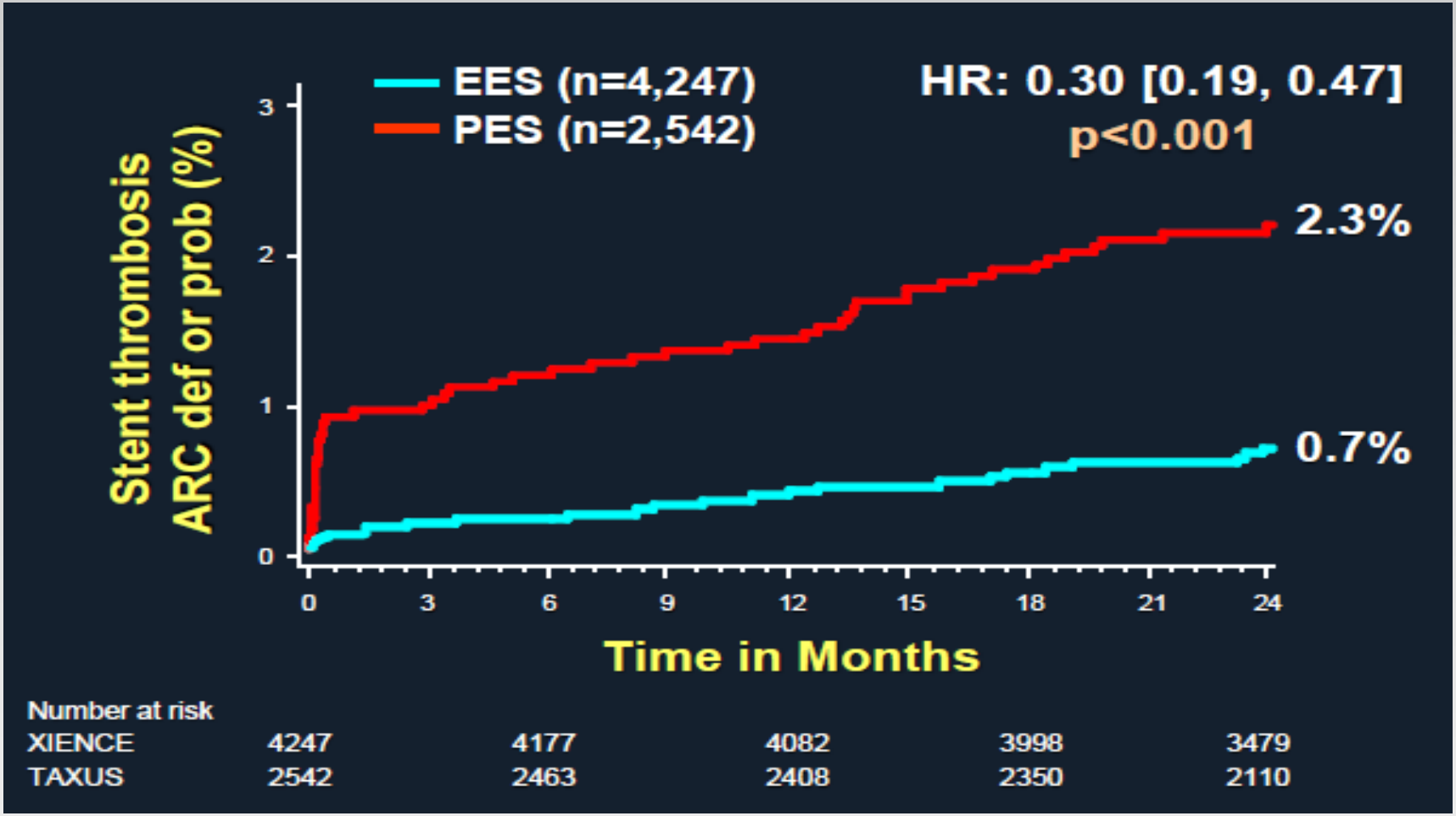
2.Generation, Aufbau



Drug-eluting stents (DES)

1. Gen vs. 2.Gen. Stents

SPIRIT II-IV, COMPARE, Stentthromboserate

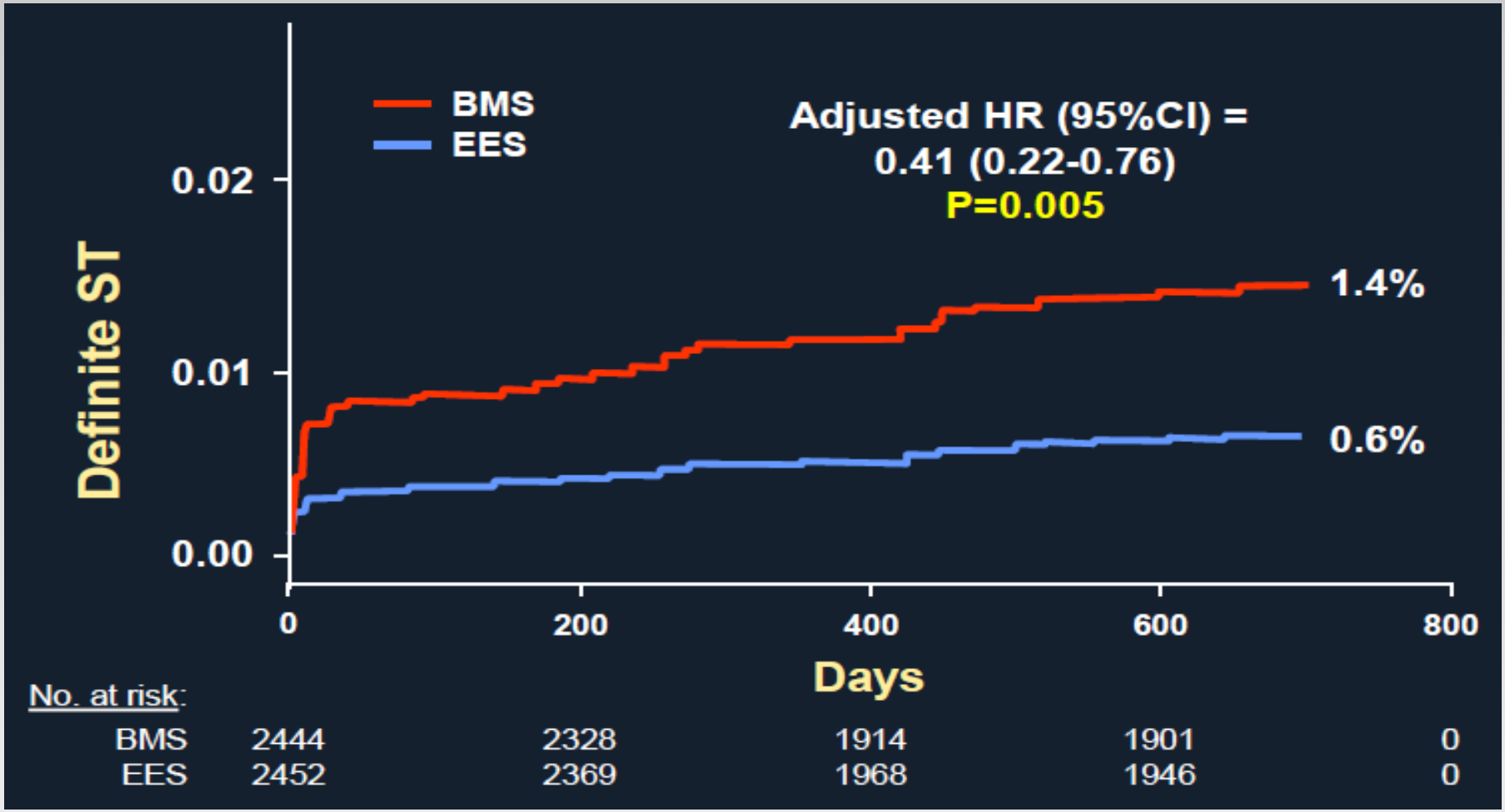


Kereaikes et al. EuroIntervention 2011

Drug-eluting stents (DES)

EES vs. BMS

Stentthromboserate



Valgimigli et al. EuroIntervention 2014

Drug-Eluting Stents (DES)

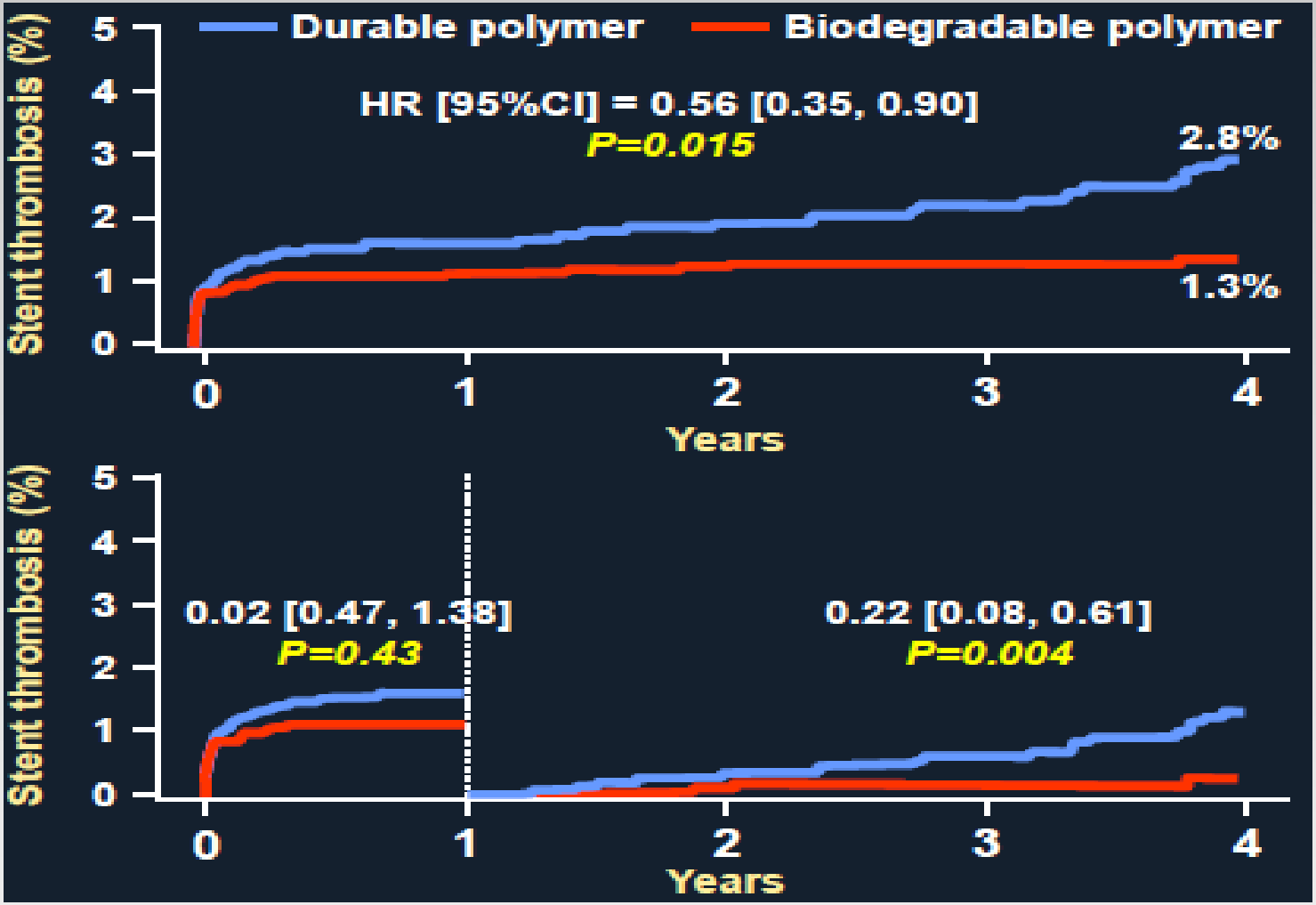
Weitere Verbesserung der Materialtechnik ?

- Metallische DES mit resorbierbarem Polymer
- Polymerfreie metallische DES
- Komplett resorbierbare Stent (Scaffolds, BVS)

Drug-Eluting Stents (DES)

Resorbierbares Polymer (4 RCTs, n=4066)

Meta-Analyse Biolimus A9 vs. Sirolimus (Cypher)



Steffanini et al. Eur Heart J 2014

Polymerfreie DES (Biofreedom)

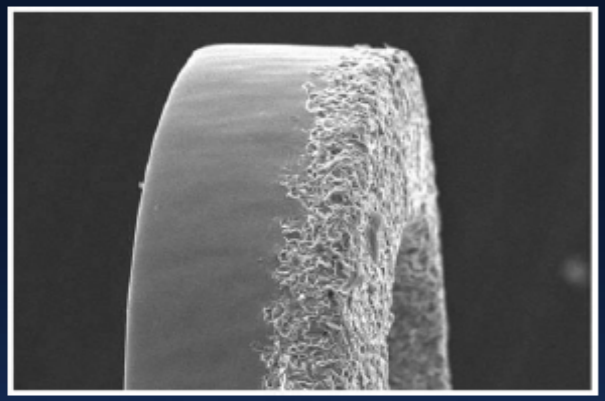
BioFreedom Stent (Biosensors)

Hypothesis: Polymer-free drug release via porous-eluting stents may reduce late events caused by polymer stent coatings.

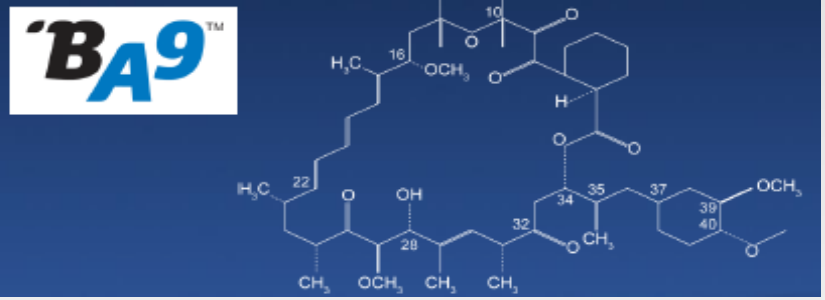
Potential advantages

- Avoid long term late adverse effects that might be attributable to the polymer
- Improved surface integrity since there is no polymer to be sheared or pealed away from the stent struts
- Possible shorter need of dual antiplatelet therapy

Selectively micro-structured surface holds drug in abluminal surface structures



Biolimus A9 - lipophilic



Urban P TCT 2015

Polymerfreie DES (Biofreedom)

LEADERS FREE Trial Design

Prospective, double-blind randomized (1:1) trial
2466 High bleeding risk (HBR) PCI patients

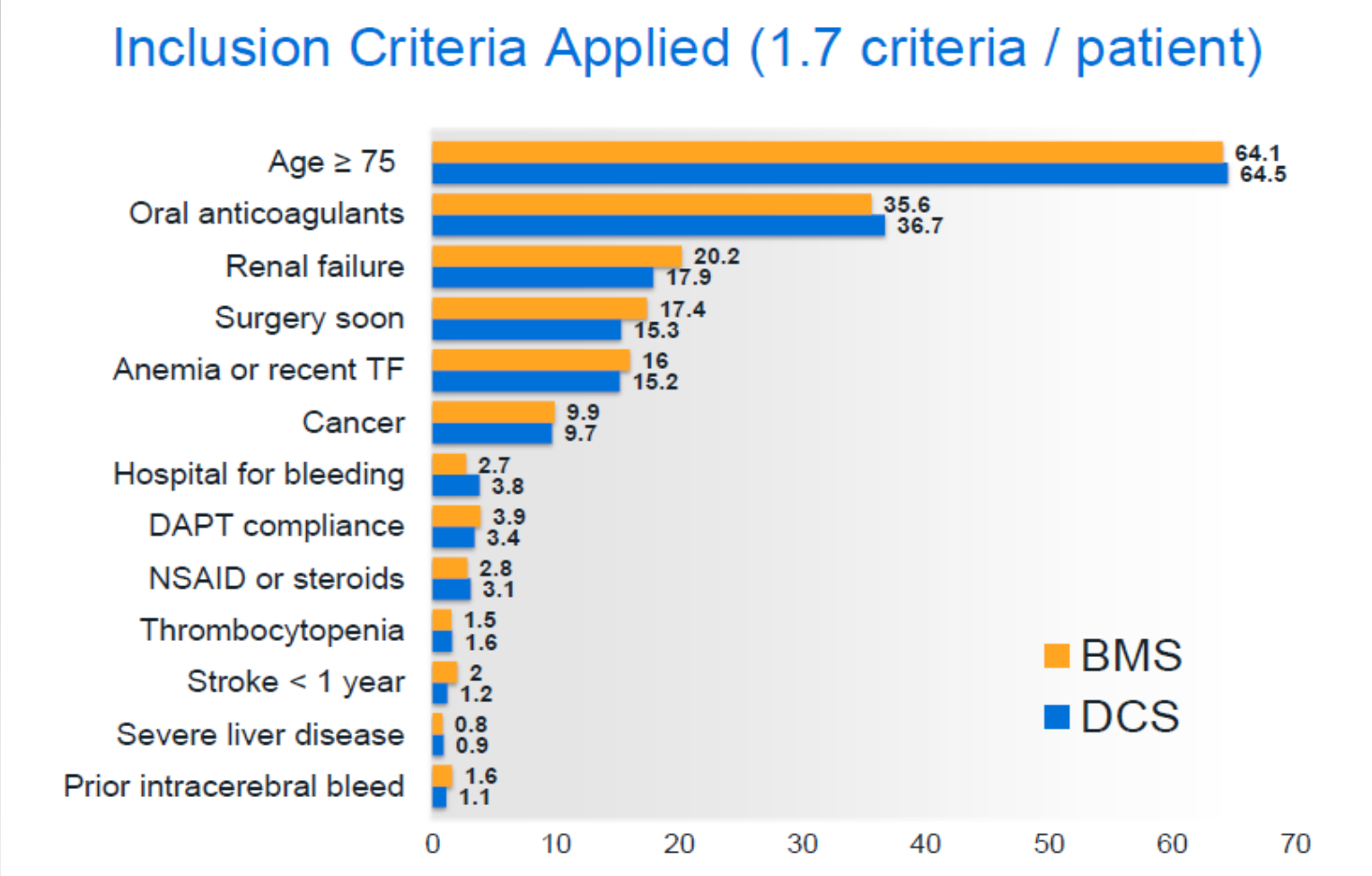
BioFreedom™ DCS	vs.	Gazelle™ BMS

DAPT mandated for 1 month only, followed by long-term SAPT

- **Primary safety endpoint:**
  Composite of cardiac death, MI, definite / probable stent thrombosis at 1 year (non-inferiority then superiority)
- **Primary efficacy endpoint:**
  Clinically-driven TLR at 1 year (superiority)

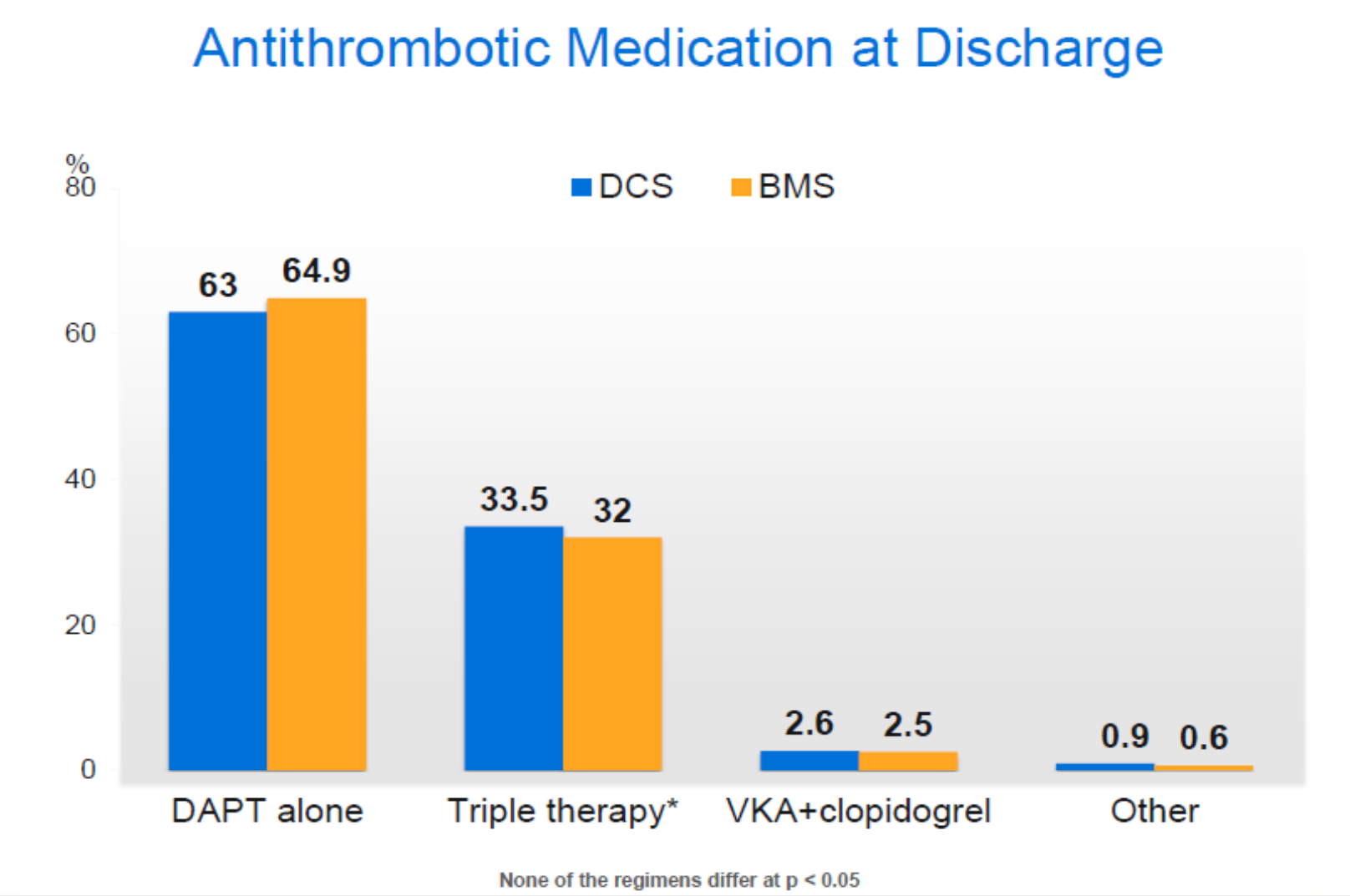
Urban P TCT 2015

Polymerfreie DES (Biofreedom)



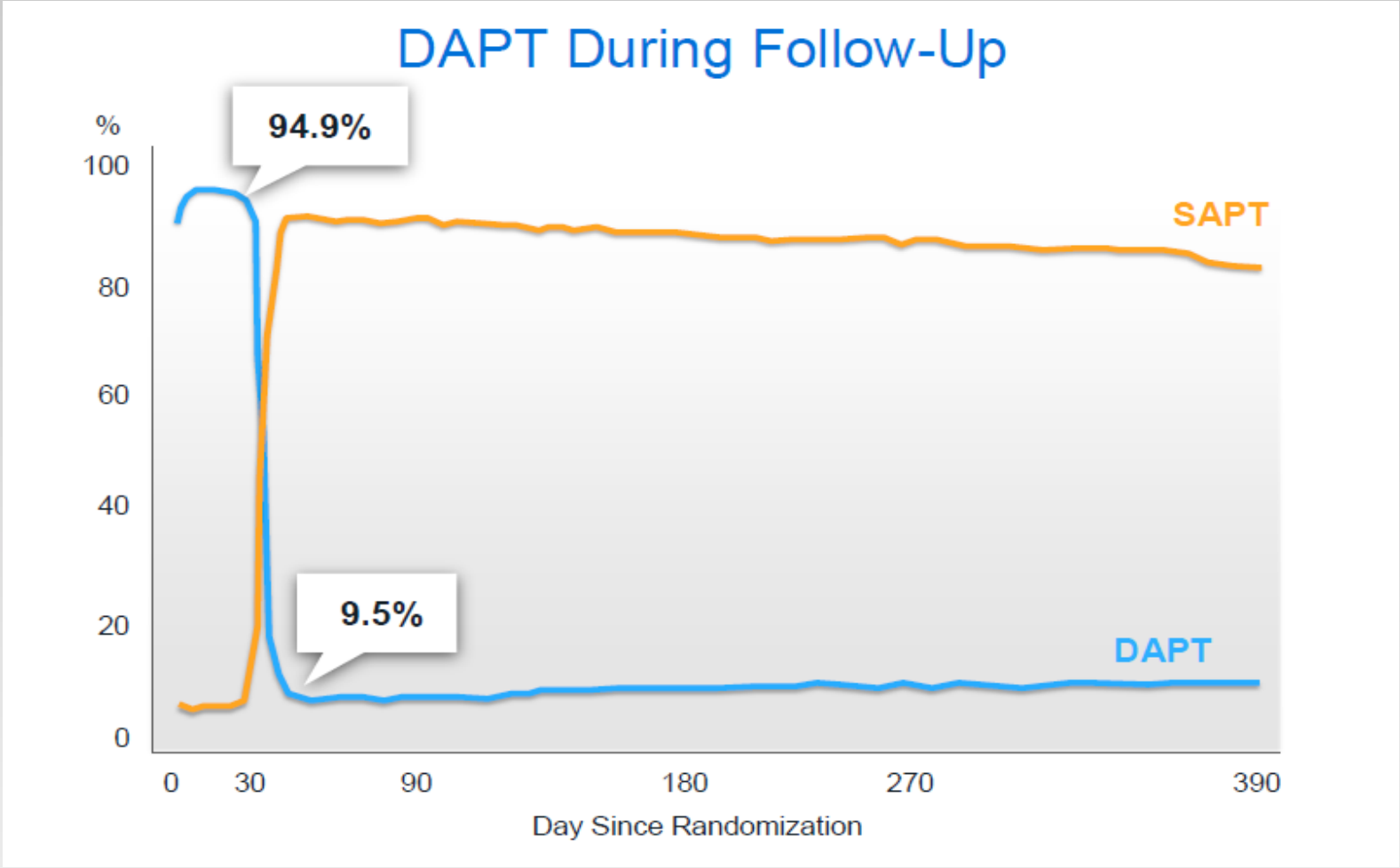
Urban P TCT 2015

Polymerfreie DES (Biofreedom)



Urban P TCT 2015

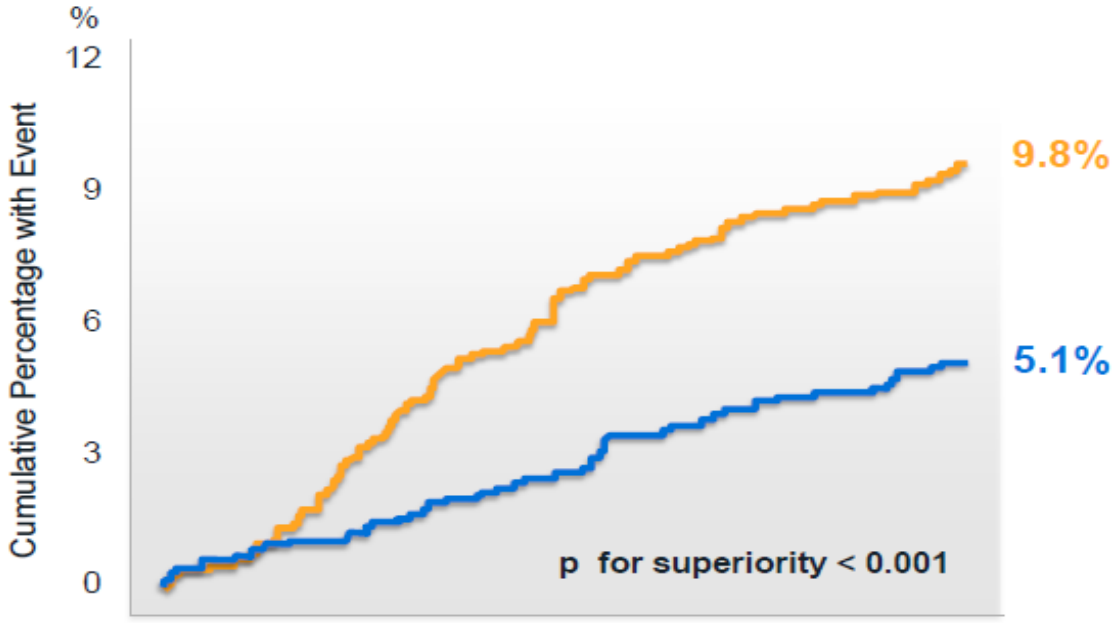
Polymerfreie DES (Biofreedom)



Urban P TCT 2015

Polymerfreie DES (Biofreedom)

Primary Efficacy Endpoint (Clinically-Driven TLR)

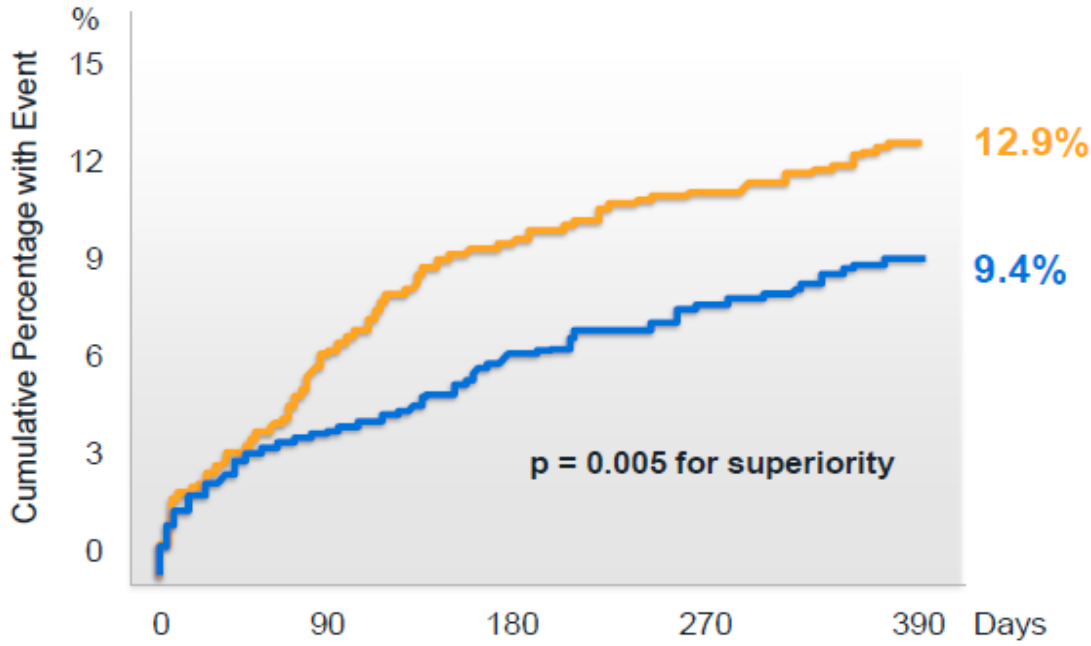


Number at Risk					
DCS	1221	1167	1130	1098	1053
BMS	1211	1131	1072	1034	984

Urban P TCT 2015

Polymerfreie DES (Biofreedom)

Primary Safety Endpoint (Cardiac Death, MI, ST)

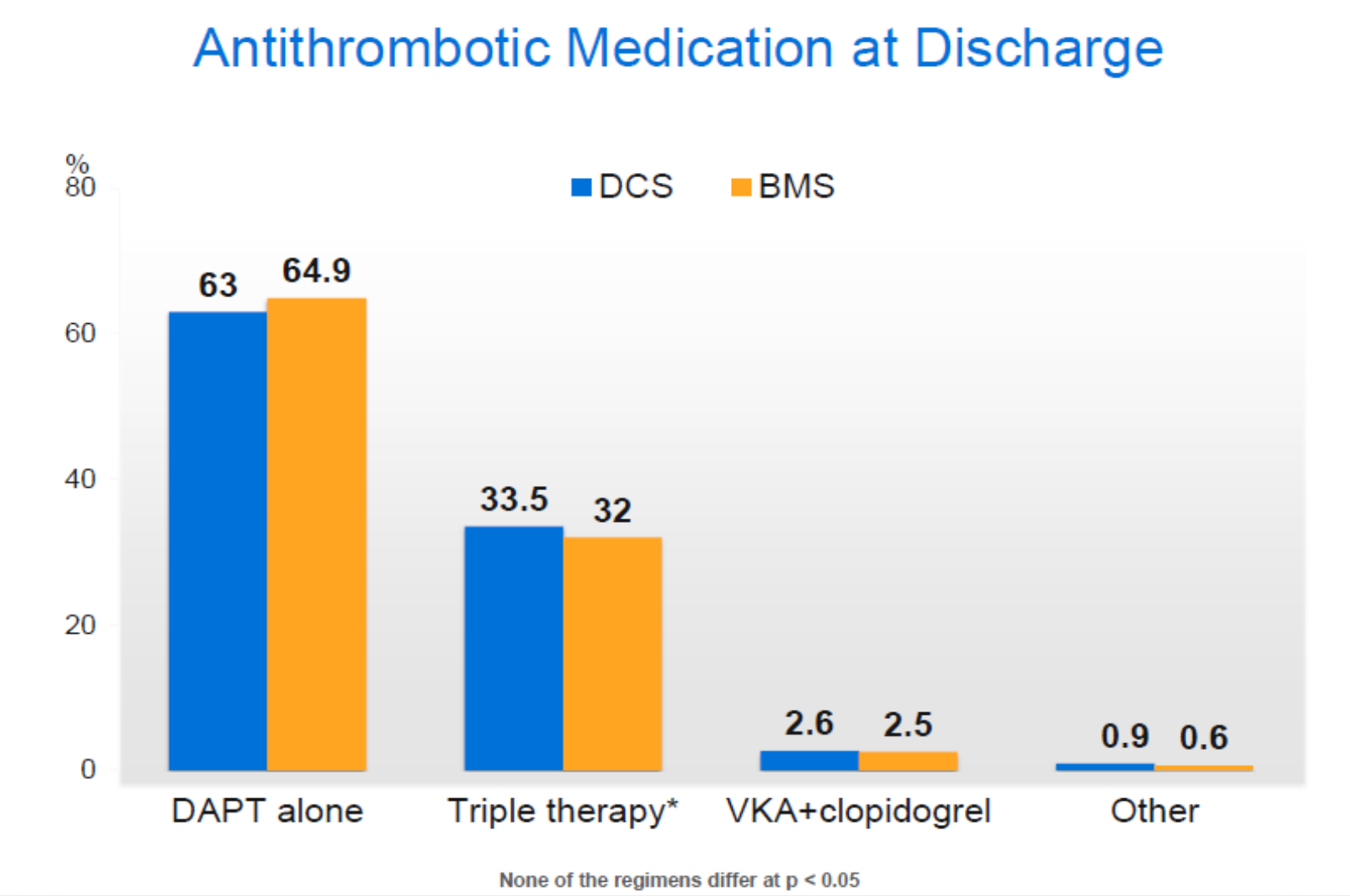


Number at Risk

DCS	1221	1146	1105	1081	1045
BMS	1211	1115	1066	1037	1000

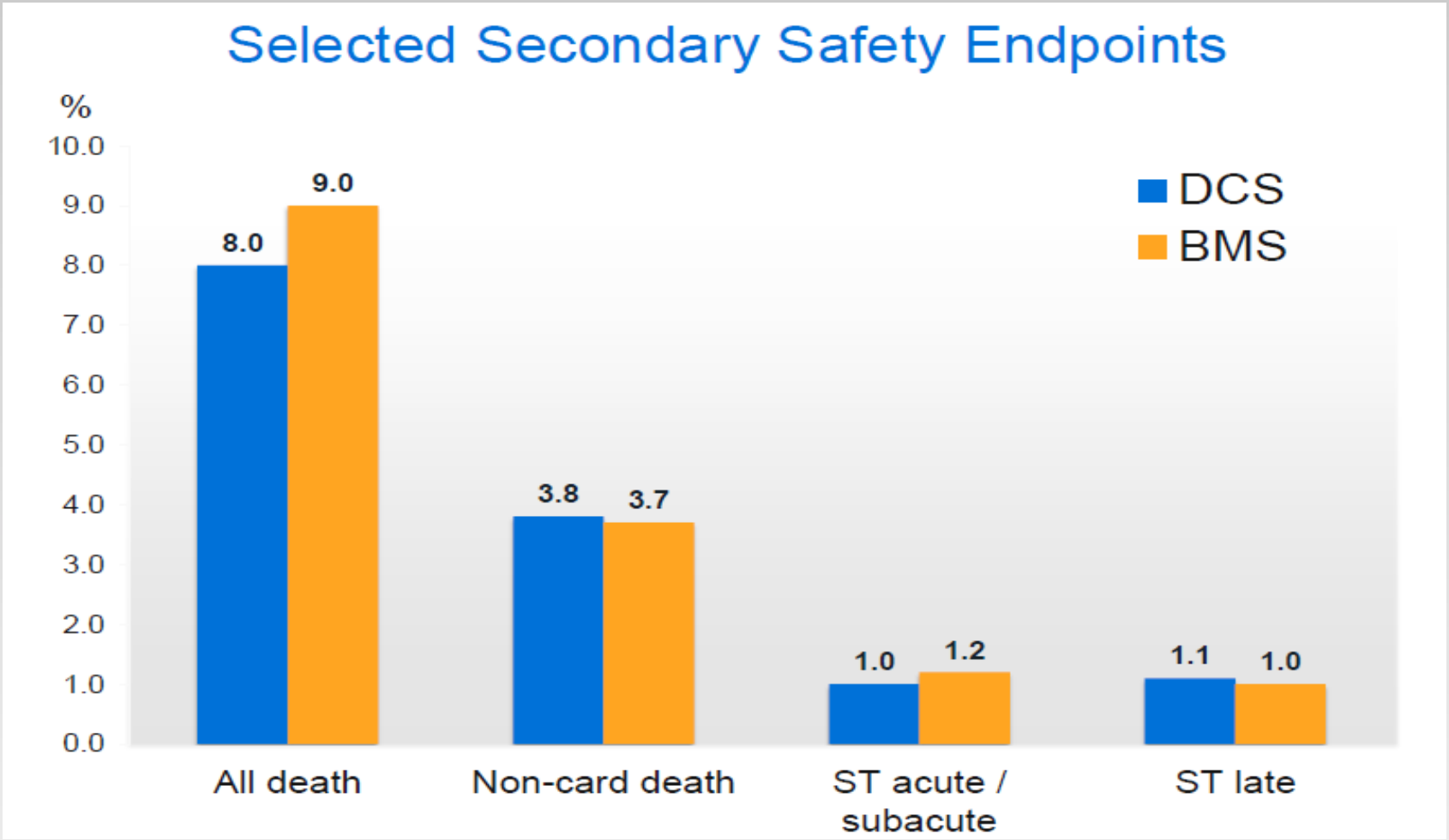
Urban P TCT 2015

Polymerfreie DES (Biofreedom)



Urban P TCT 2015

Polymerfreie DES´(Biofreedom)



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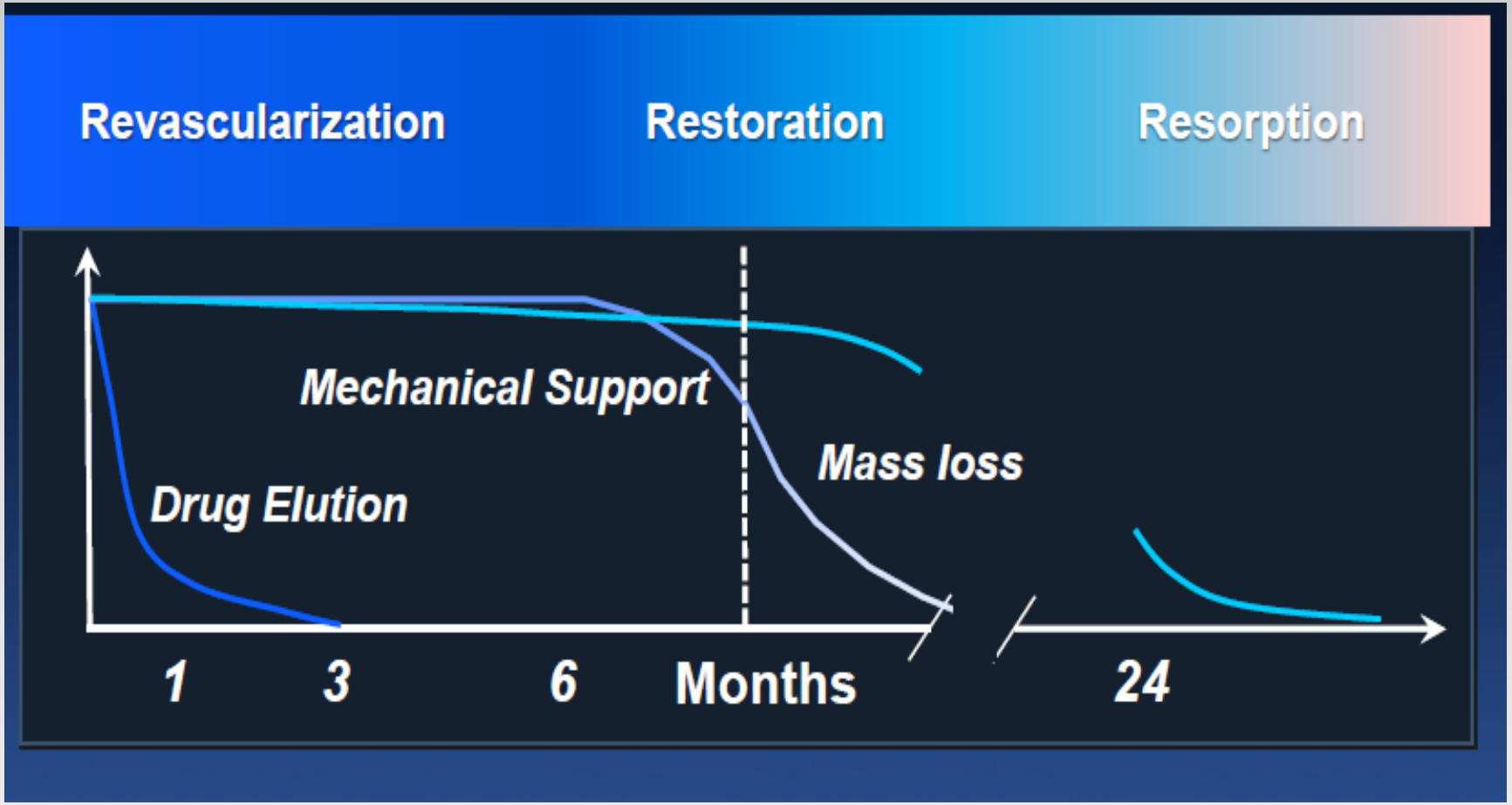
Bioresorbierbare Scaffolds (BVS)

Absorb III, Aufbau

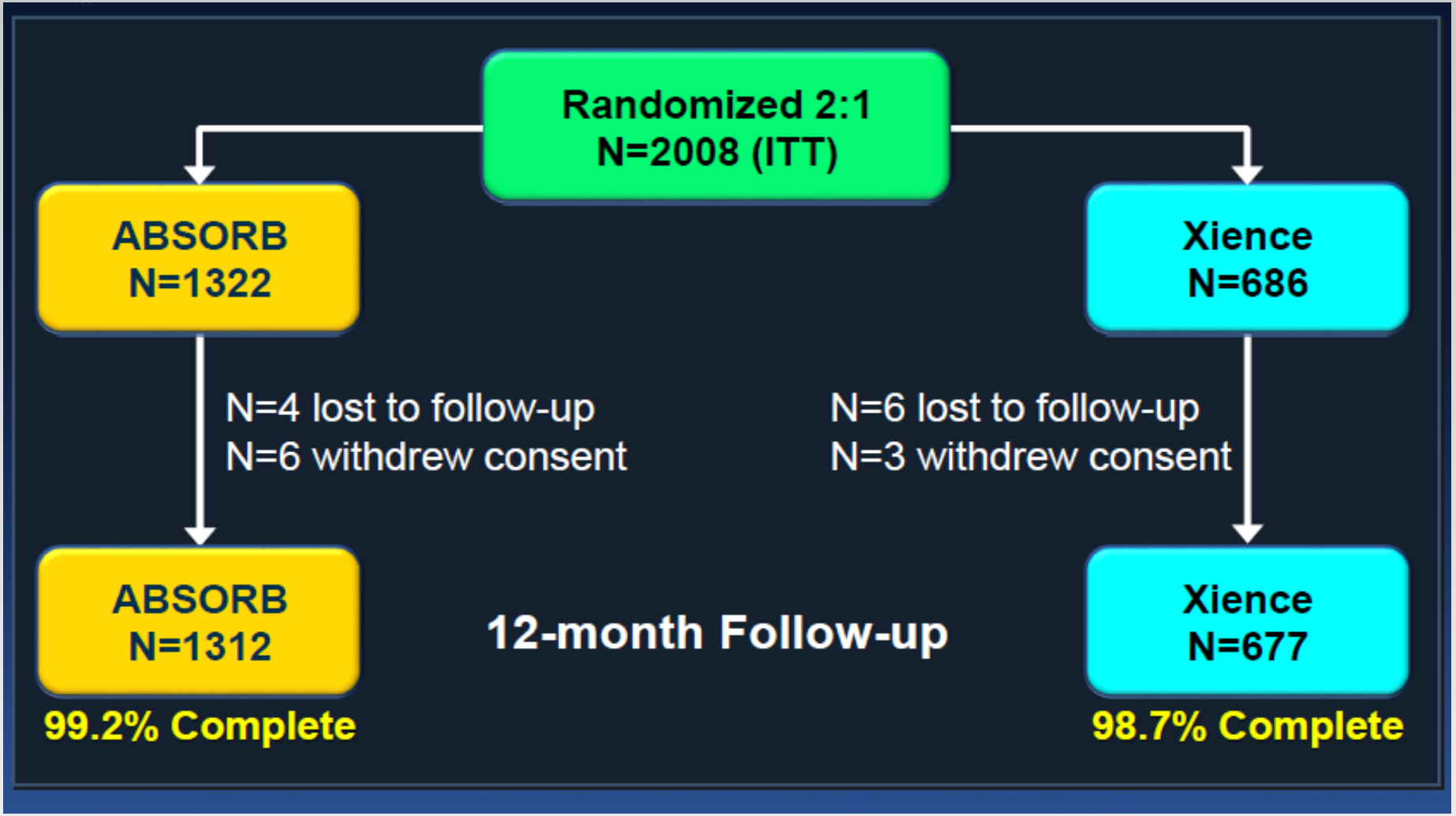
Bioresorbierbare Scaffolds (**BVS**)

Absorb III, Resorptionskinetik



Bioresorbierbare Scaffolds (**BVS**)

Absorb III



Bioresorbierbare Scaffolds (BVS)

Absorb III, Stentthrombosen

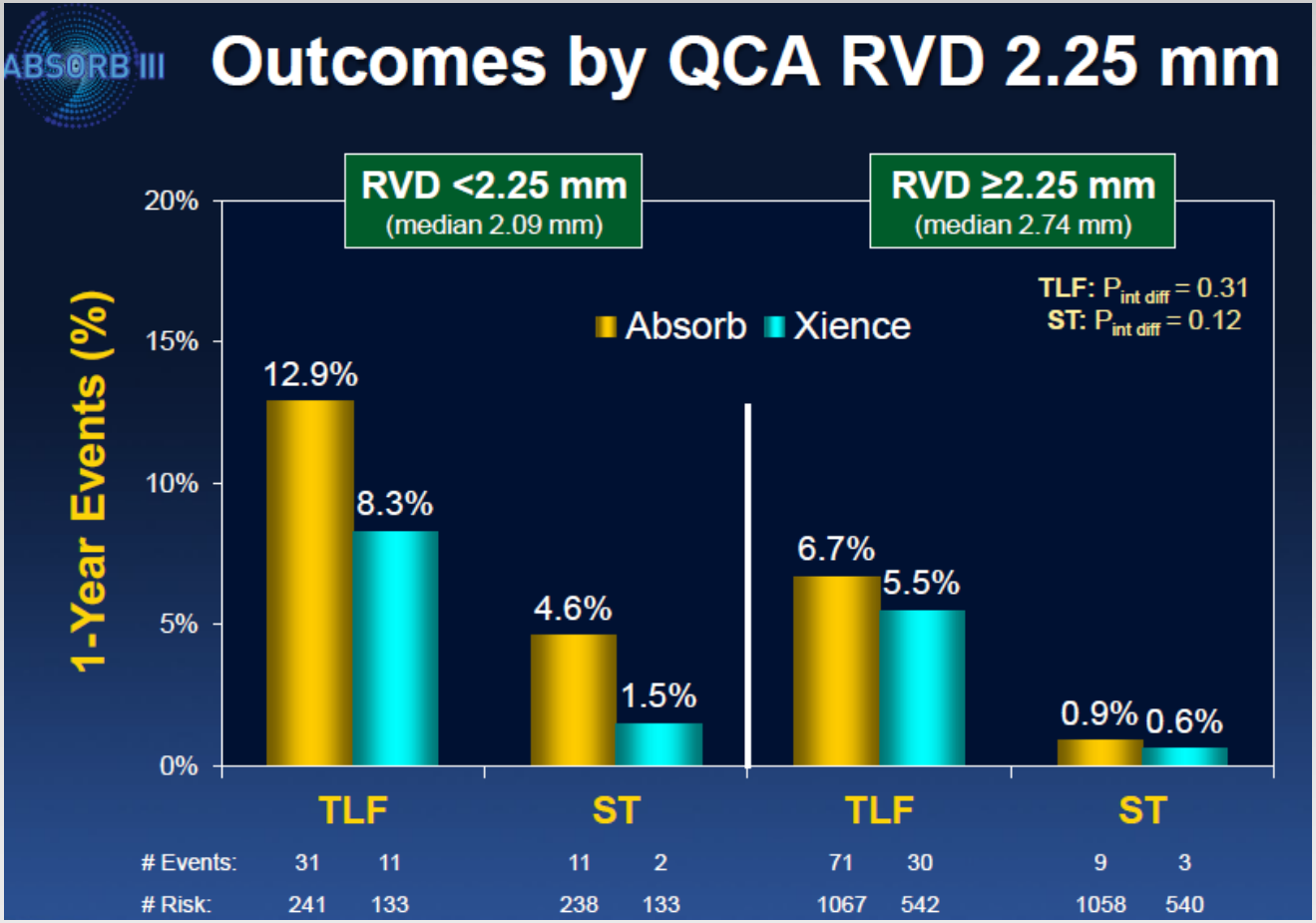
Device Thrombosis to 1 Year

	Absorb (N=1322)	Xience (N=686)	p-value
Device Thrombosis (def*/prob)	1.54%	0.74%	0.13
- Early (0 to 30 days)	1.06%	0.73%	0.46
- Late (> 30 to 1 year)	0.46%	0.00%	0.10
- Definite* (1 year)	1.38%	0.74%	0.21
- Probable (1 year)	0.15%	0.00%	0.55

*One "definite ST" in the Absorb arm by ITT was in a pt that was treated with Xience

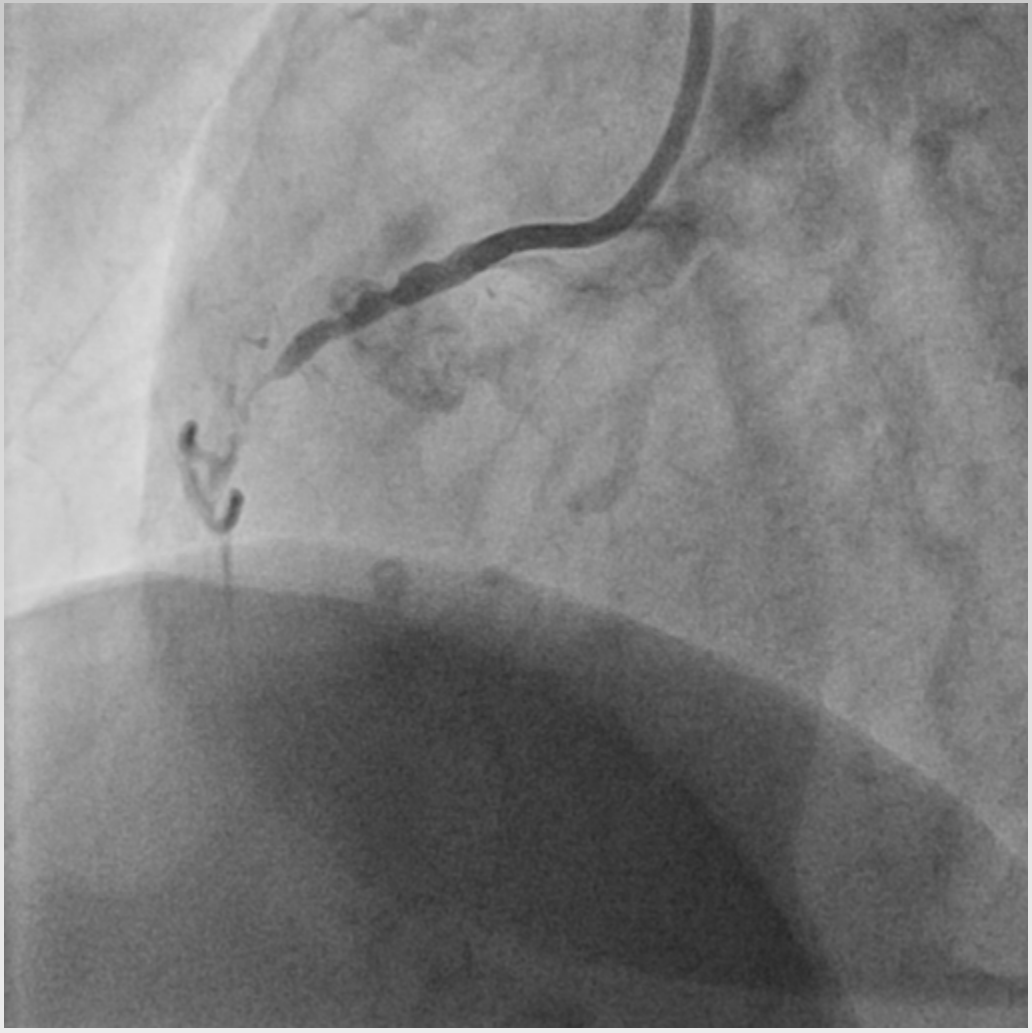
Bioresorbierbare Scaffolds (BVS)

Absorb III, Stentthrombosen
kleine vs. Grosse Gefäße

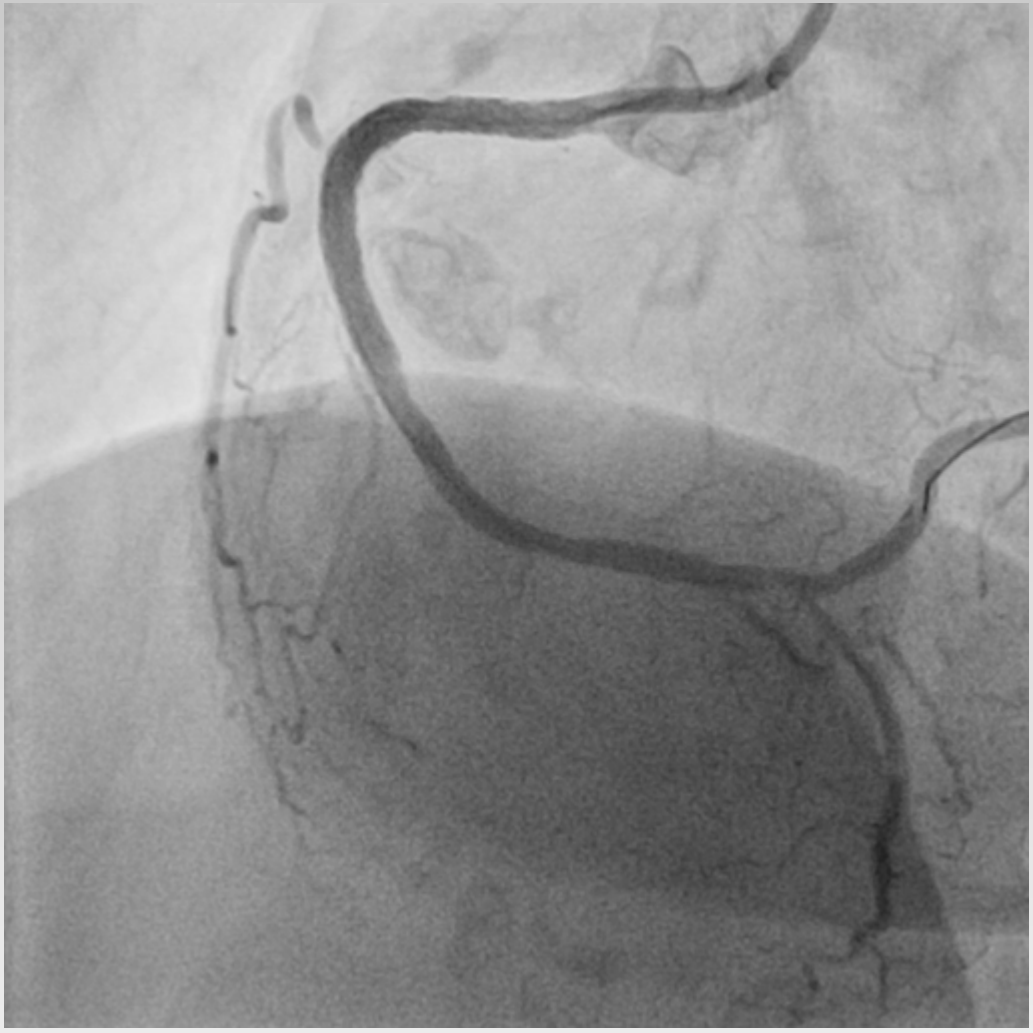


A.H, 81-Jahre, stabile AP CCS IV

KHK-3, Hauptstammstenose



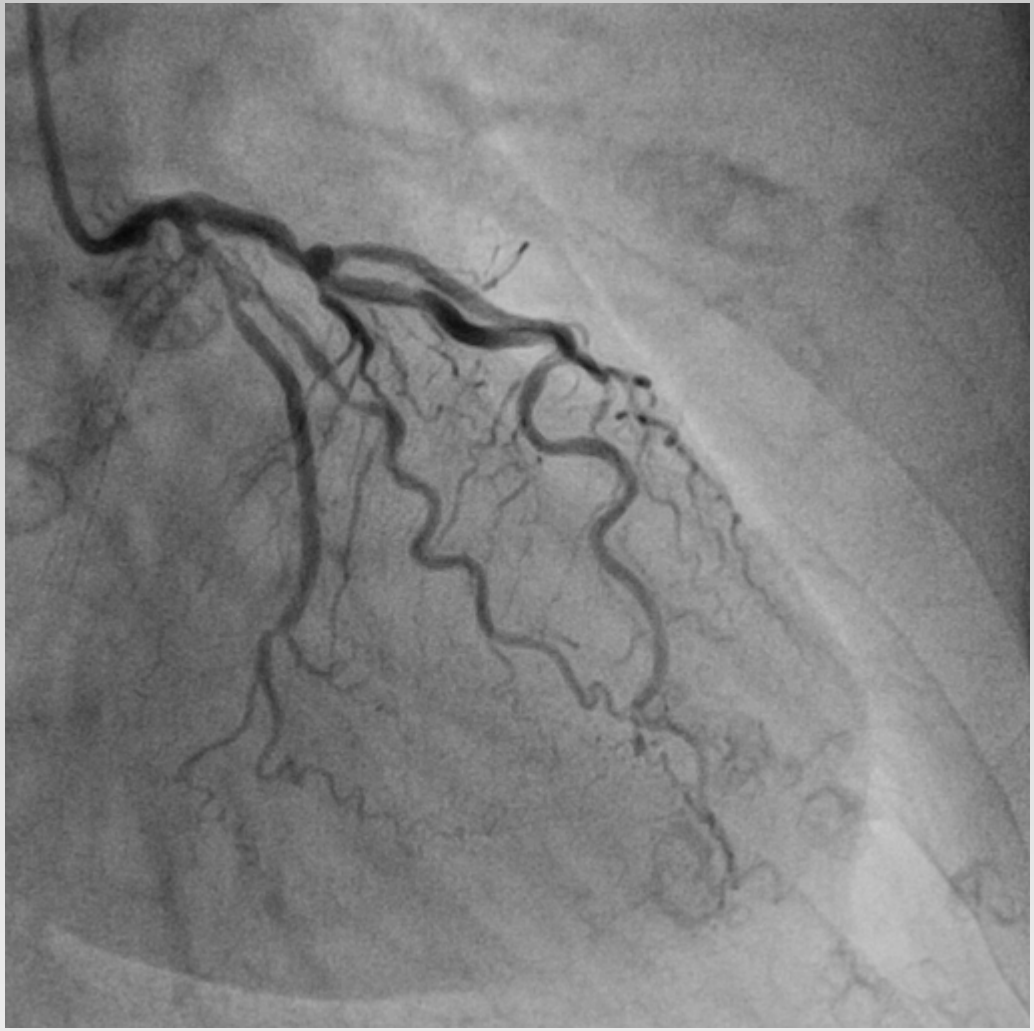
Chronischer Verschluss RCA-1/2

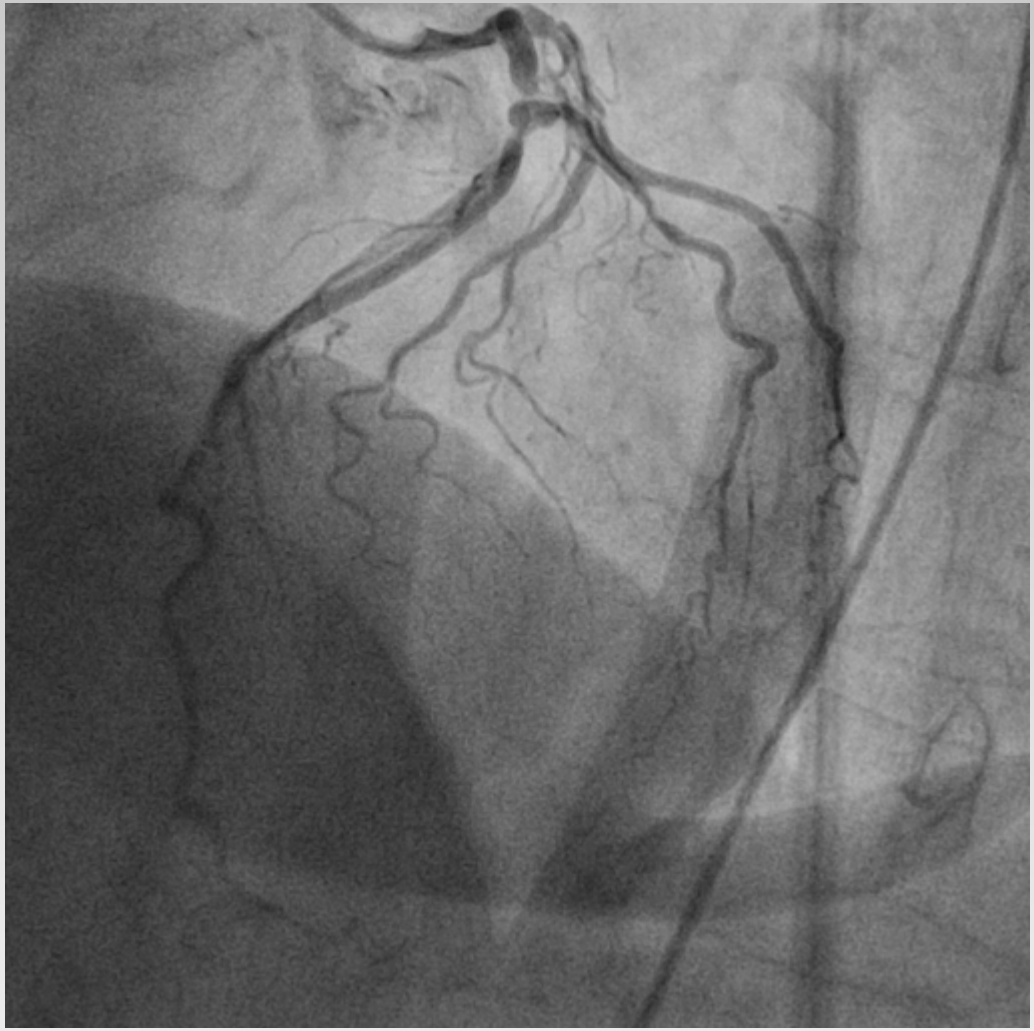


2 DES Biotrix Flex 3,5/33+28mm 16 bar

A.H, 81-Jahre, stabile AP CCS IV

KHK-3, Hauptstammstenose

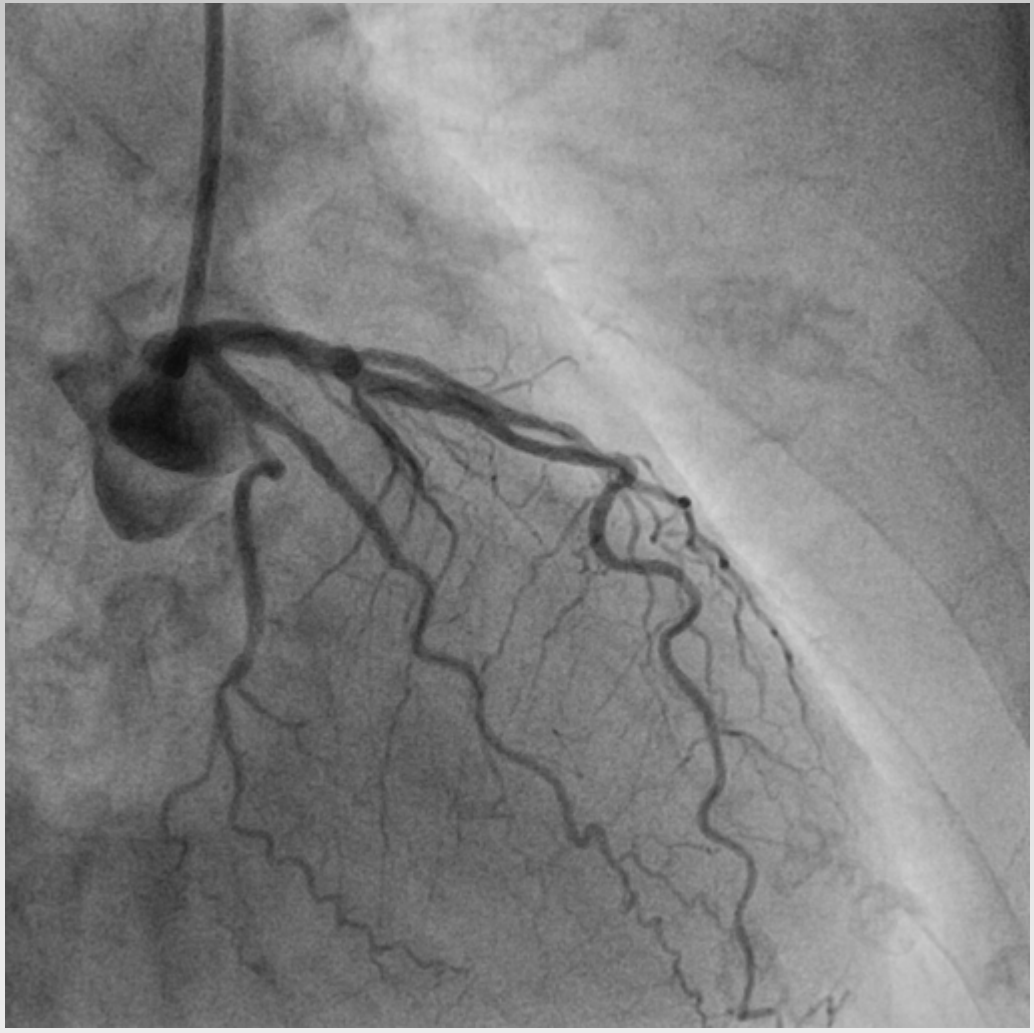


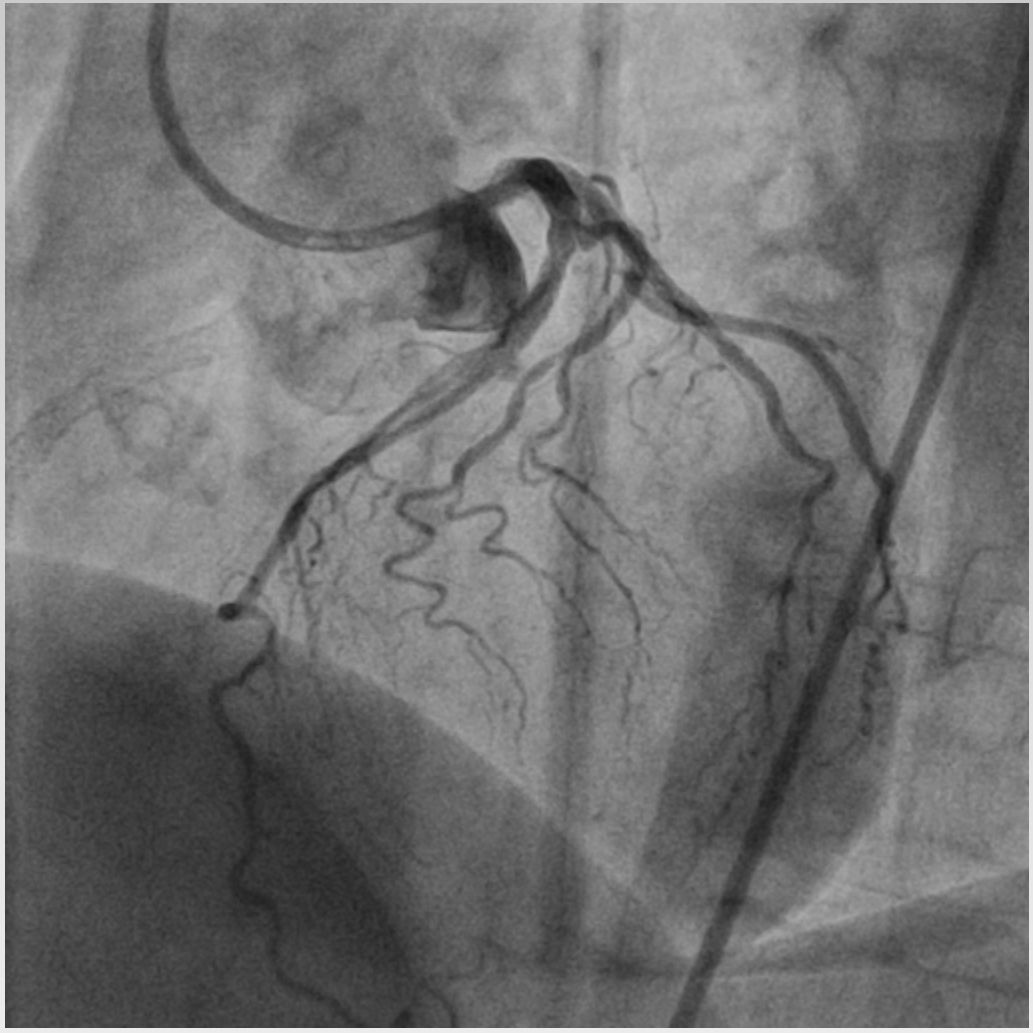


LM 50-75%, LAD-6 75%, LCX-11 75%, RCA-1/2 100%

A.H, 81-Jahre, stabile AP CCS IV

KHK-3, Hauptstammstenose

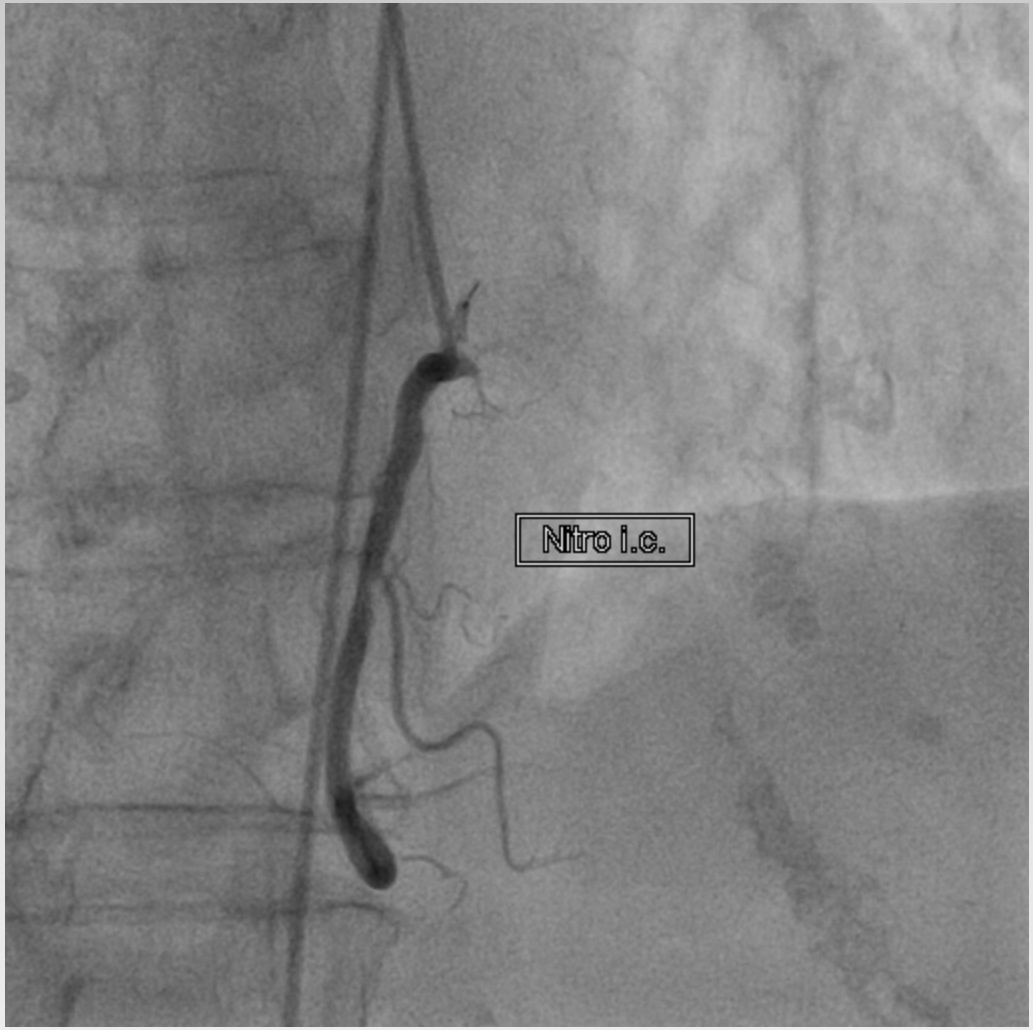




3 DES: LAD-6 Biomatrix Flex 3,5/18, LM/LAD-6/LCX-11 Mini-Crush Biomatrix Flex 3,5/14+2,5/33mm

R.H, 78-Jahre, stabile AP CCS II

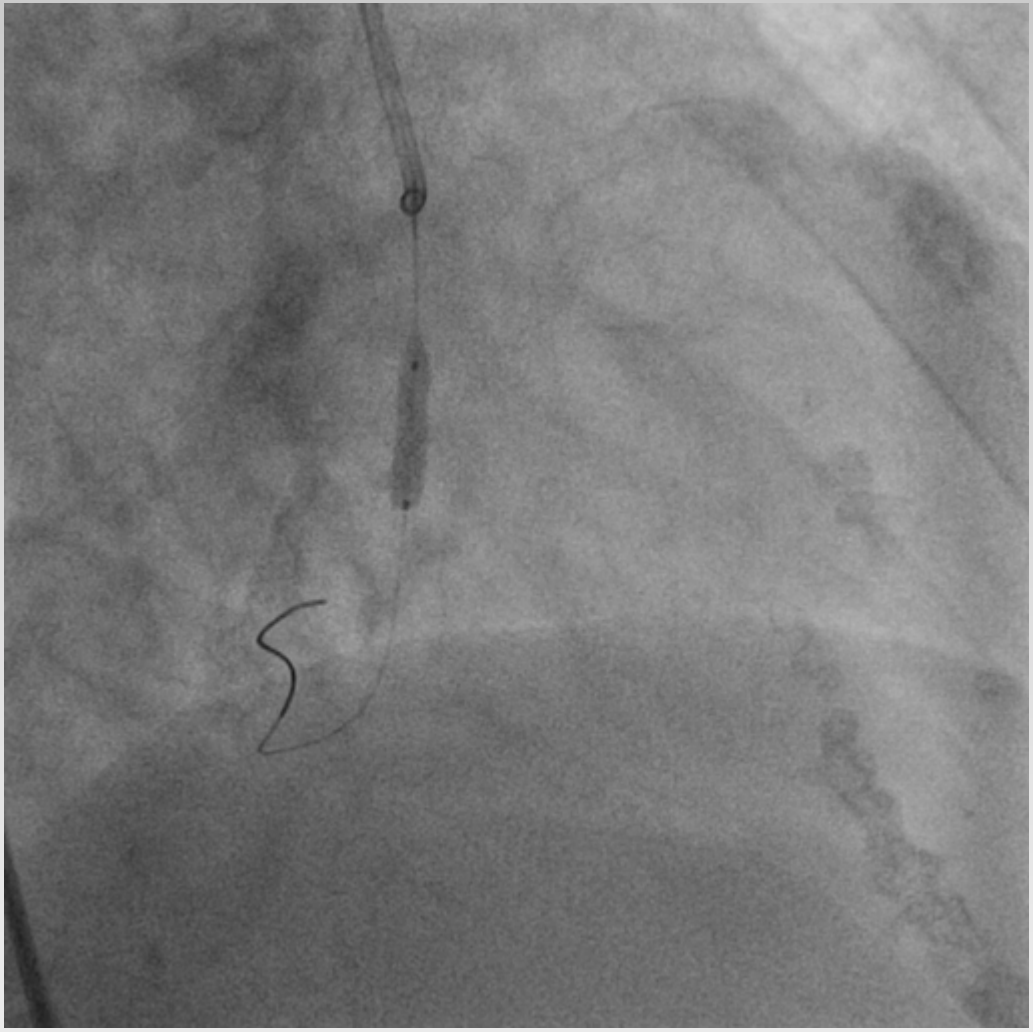
KHK-1

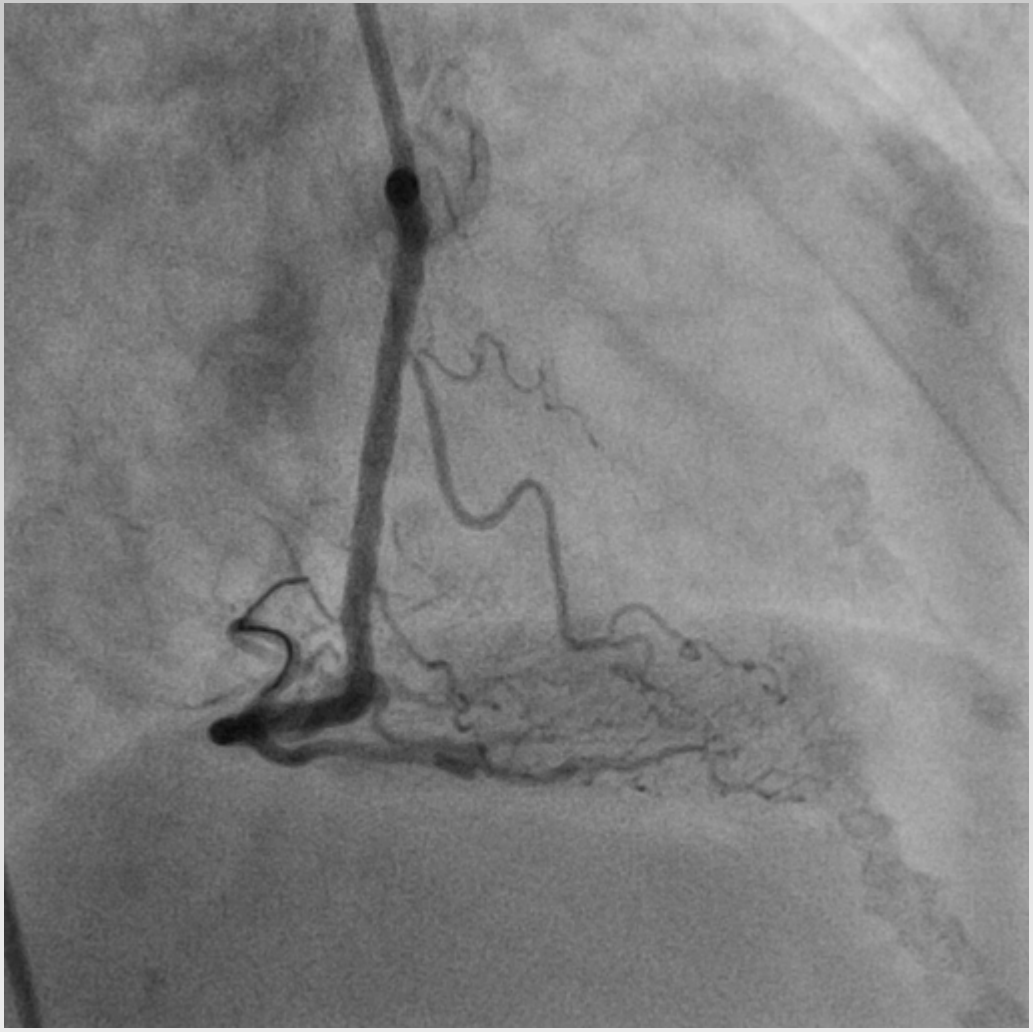


RCA-2 75%

R.H, 78-Jahre, stabile AP CCS II

KHK-1





DES 3,5/12mm Promus Element

Zusammenfassung I

- Nach elektiver DE-Stentimplantation der 2.Generation ist eine duale Plättchenhemmung (DAPT = ASS+Clopidogrel) von 6 Monaten ausreichend.
- Nach elektiver DE-Stentimplantation der 2.Generation unter DAPT über 6 Monate ist eine späte Stentthrombose extreme selten und vergleichbar häufig oder seltener als nach BMS-Implantation.
- Eine längere DAPT über 6 Monate sollte nur in Ausnahmefällen nach Rücksprache/Empfehling des interventionellen Zentrums verordnet werden.

Zusammenfassung II

- Bei Verwendung polymerfreier DE-Stents (Biofreedom) kann eine DAPT von nur 1 Monat vertreten werden.
- BVS (medikamntenfreisetzende bioresorbierbare Stents) sollten aufgrund der limitierten Datenlage auf grosse Koronargefäße (> 2,5mm) beschränkt werden und mindestens über 6 Monate mit DAPT behandelt werden.

Zusammenfassung III

- Grundvoraussetzung für eine langfristig sichere und effektive koronare Stentimplantation jeglicher Bauart (BMS/DES/BVS) ist eine sorgfältige Implantation (Läsionsvorbereitung, adequate Größenauswahl, Hochdruckimplantation) durch den interventionellen Kardiologen !!