PtCr EES, Beyond PROMUS Element™

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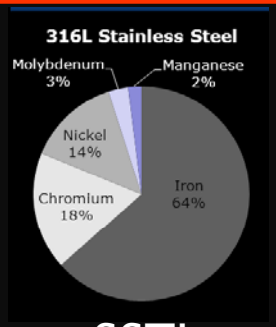
Desired Features of Next Generation DES

Next Generation DES Desired Attributes	SYNERGY™ Stent Attributes and Design Goals
Acute Performance Deliverable Visible Trackable Conformable	**Stent & Delivery System** PtCr Stent Platform Thin Struts Modified Cell Geometry Improved Deliverability
Efficacy Good Clinical Outcomes Low TLR Low Clinical Symptom Recurrence	**Low Drug Load** Drug Load = PROMUS™/Xience™ Release kinetics similar to PROMUS™/Xience™
Safety No Stent Thrombosis Shortened DAPT Requirement Safer for DAPT Interruption	**Reduced Polymer Load** Bioabsorbable Polymer BMS within 4mo Abluminal Polymer Coating Low Polymer Mass

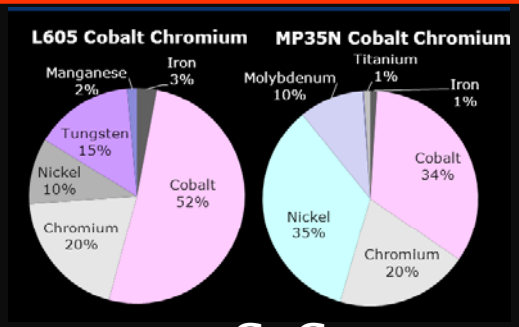
Presented by Ian Meredith AM, MBBS PhD, TCT 2011 The SYNERGY™ Stent System is an investigational device and not for sale.

Stent Design Progression: Platform

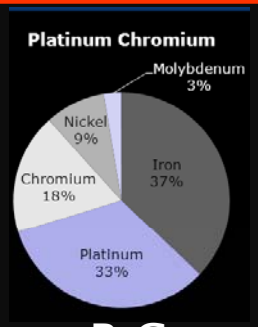
Material



SSTL



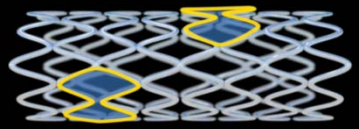
CoCr



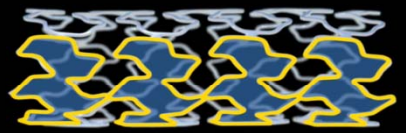
PtCr

Architecture

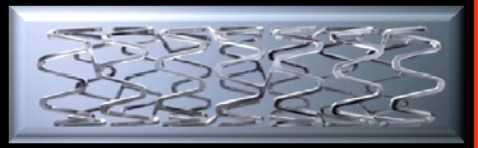
Closed Cell / Strength



Open Cell / Flexibility



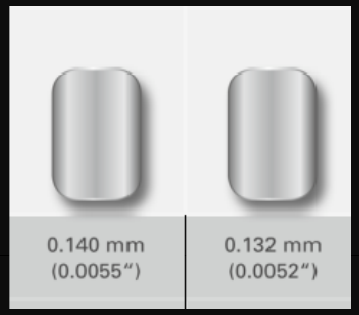
Hybrid / Coverage



Optimization

Strut Thickness

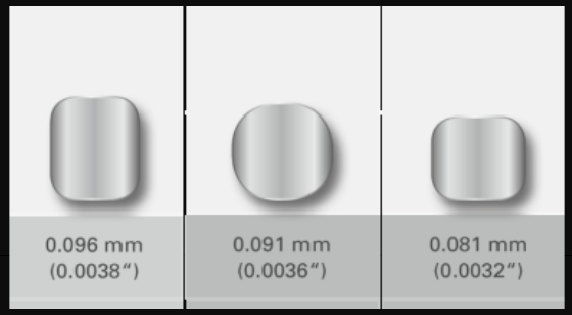
1st Generation



Cypher™ Stent

TAXUS® Express® Stent

2nd Generation

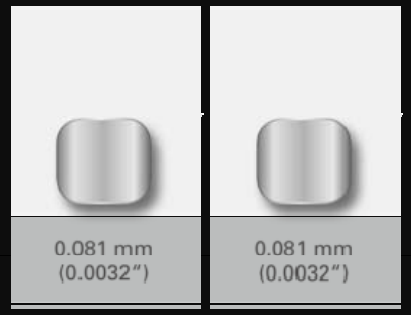


TAXUS® Liberté® Stent

Endeavor® Stent

Xience® Stent PROMUS® Stent

3rd Generation

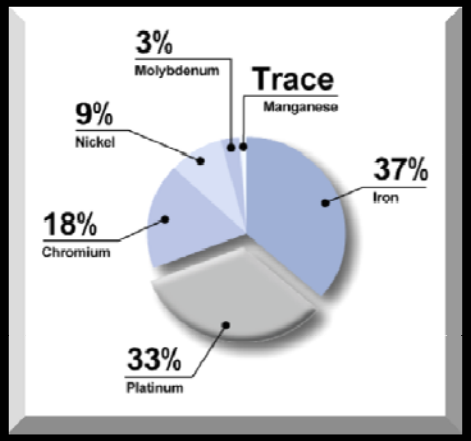


PROMUS Element™ Stent

ION™ / TAXUS™ Element™ Stent

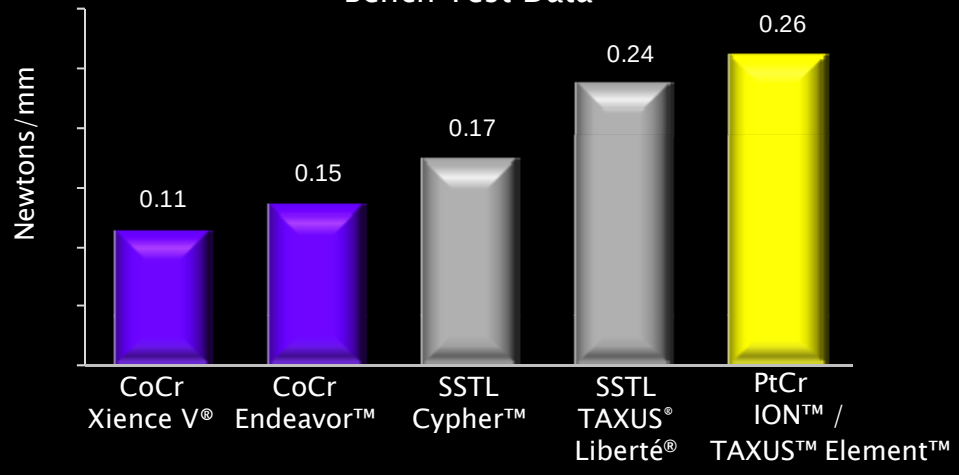
Platinum Chromium (PtCr) Stent Material

Biocompatibility



Radial Strength

Bench Test Data



Flexibility

Radiopacity

The ION™ Stent is commercialized as TAXUS™ Element™ outside the US.
Data on file at Boston Scientific. Bench test results may not necessarily be indicative of clinical performance.

Platinum Chromium (PtCr) Stent Series

Novel alloy with different drug & polymer choices

Product Name	Platform	Drug	Polymer
OMEGA™ Stent	Element	None	None
TAXUS™ Element™ / ION™ Stent	Element	Paclitaxel	Translute™ (SIBS)
PROMUS Element™ / PROMUS Element™ Plus	Element	Everolimus	PVDF-HFP PBMA

Next Generation PtCr Stent Under Development

Product Name	Platform	Drug	Polymer
SYNERGY™ Stent with bioabsorbable polymer	Synergy	Everolimus	PLGA

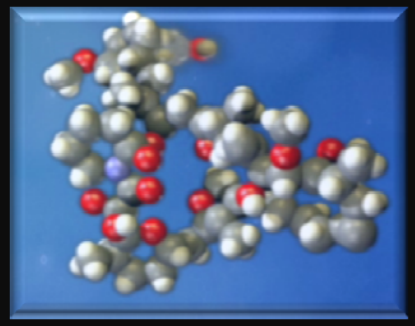
The ION™ Stent is commercialized as TAXUS™ Element™ outside the US.
The SYNERGY™ Stent System is an investigational device limited by law to investigational use. Not for sale.

Stent Design Progression: Drug Delivery

Anti-Restenotic Agents

BMS

Everolimus



DES

Polymer Coating

Biostable Conformable Polymer

Bioabsorbable Abluminal Polymer

SYNERGY™ Stent Design Goals

Bioabsorbable Polymer Theory

- Polymer only needed for controlling drug release
- Amount of polymer should be minimized
- Polymer should disappear after drug is released

SYNERGY™ Stent Design Goal

Thin abluminal bioabsorbable polymer coating designed to resorb shortly after drug delivery leaving behind a BMS

PtCr Stent Platform

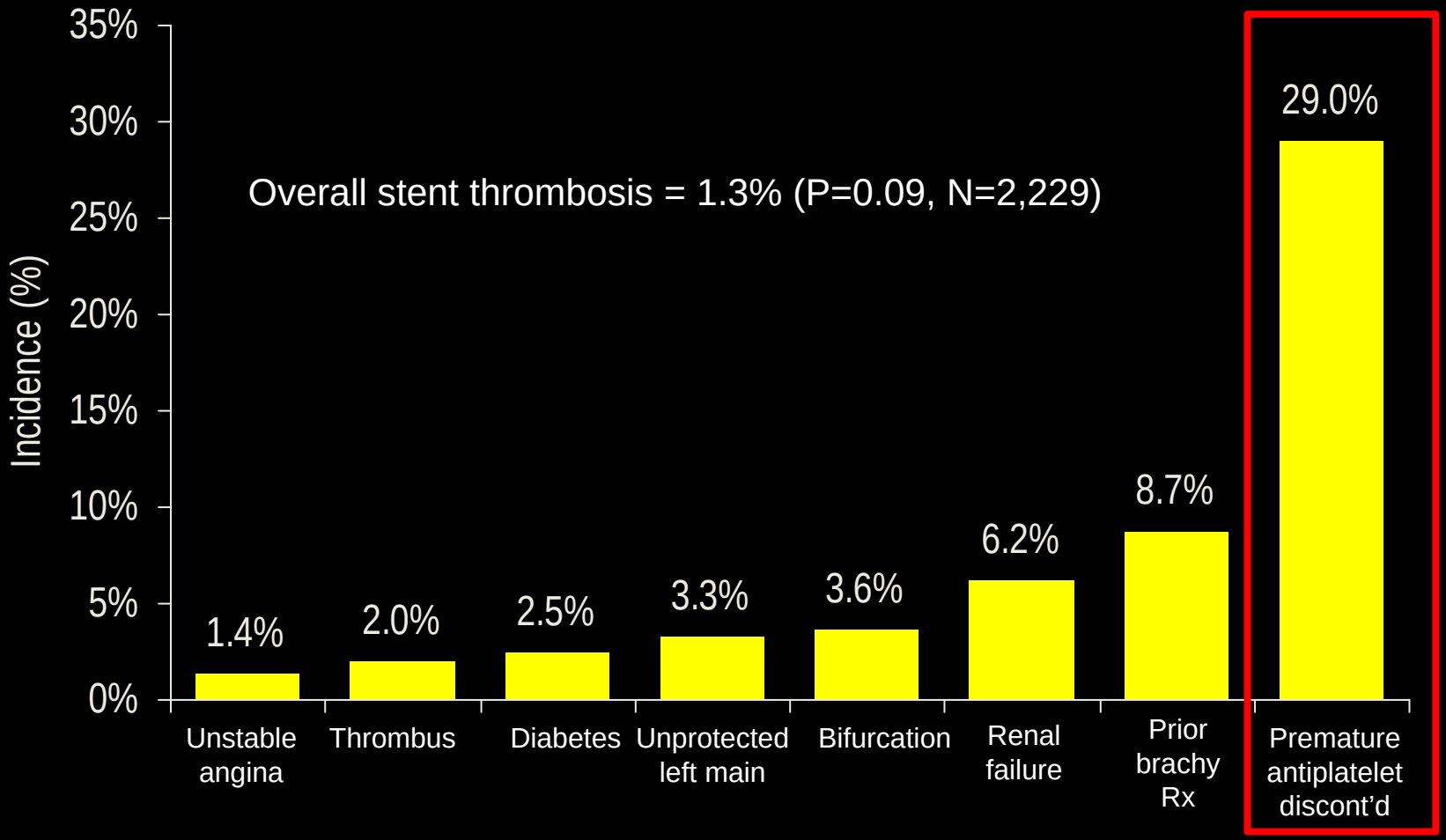
- Biocompatibility, strength, flexibility, and visibility
- Acute performance

Hypothesis

Patient can be managed like BMS–patient after polymer is gone

Modified from Ian Meredith AM, MBBS, PhD at TCT 2011. The SYNERGY™ stent is an investigational device and not for sale.

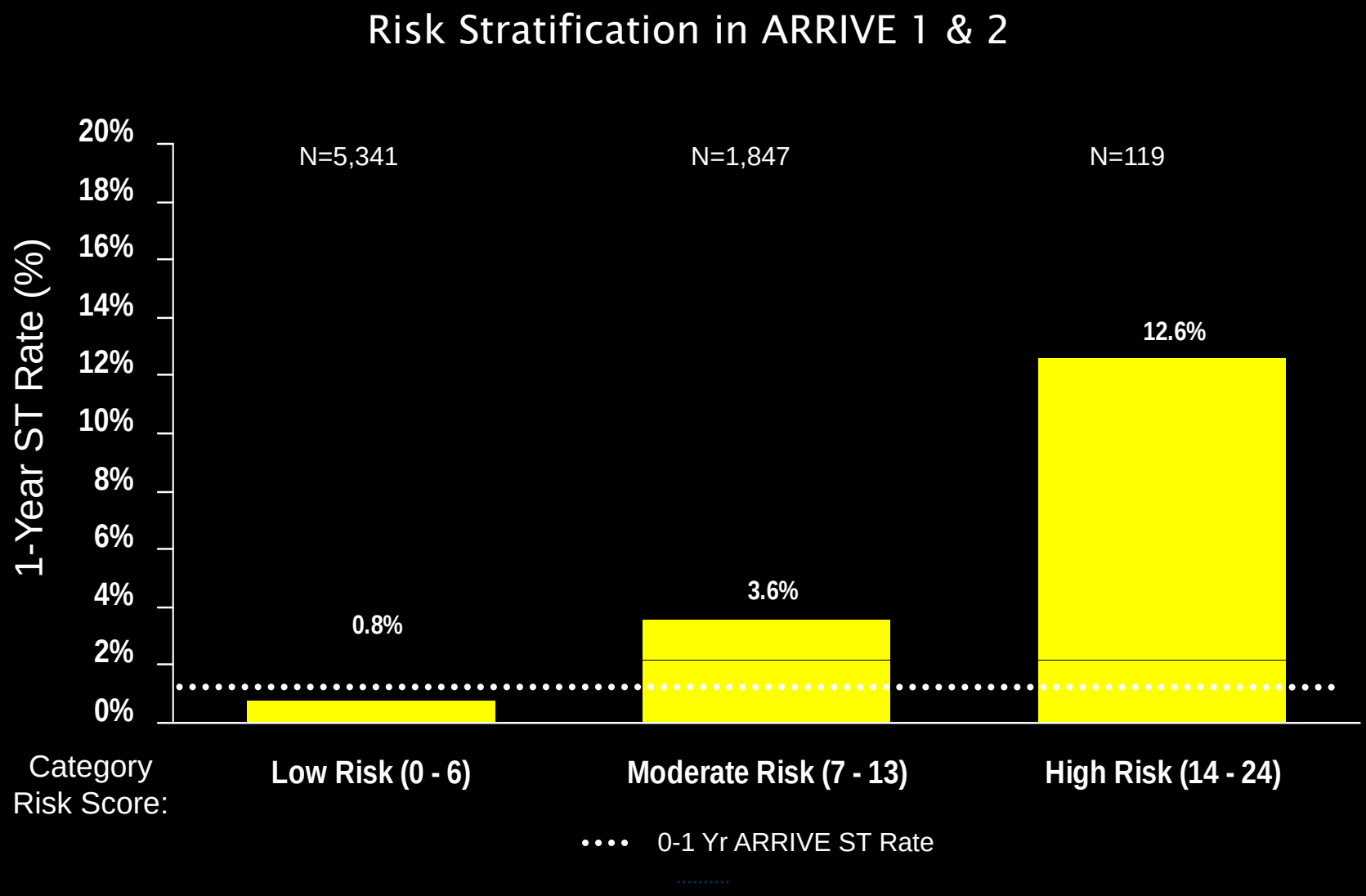
Early Discontinuation of Anti-platelet Therapy Is Strongest Risk Factor for ST with DES



Iakovou et al. JAMA. 2005;293:2126.

Not All Patients are the Same

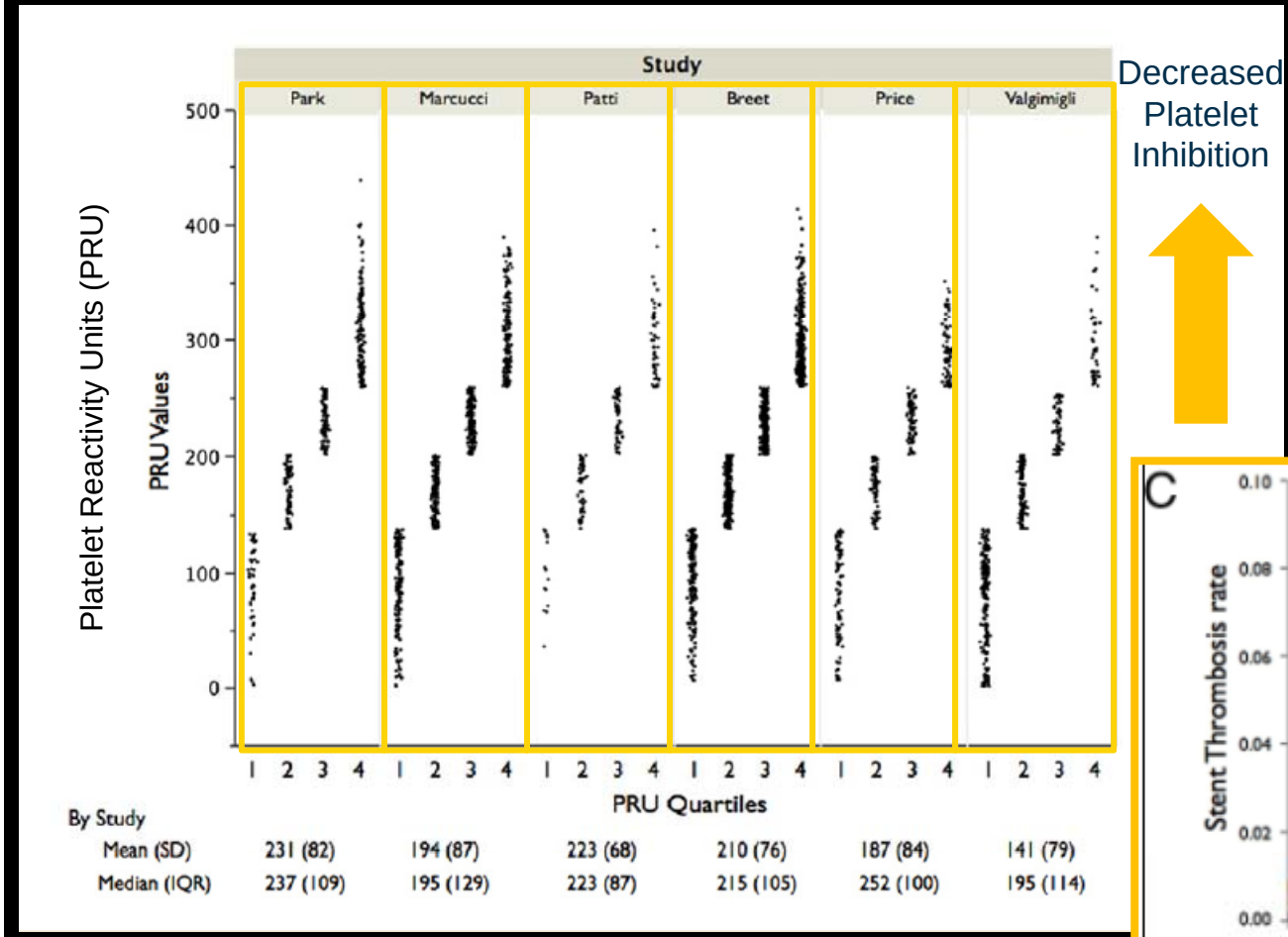
Patient Risk Profile Makes DAPT Duration Difficult to Optimize



Baran, Am J Cardiol 2008;102:541-545

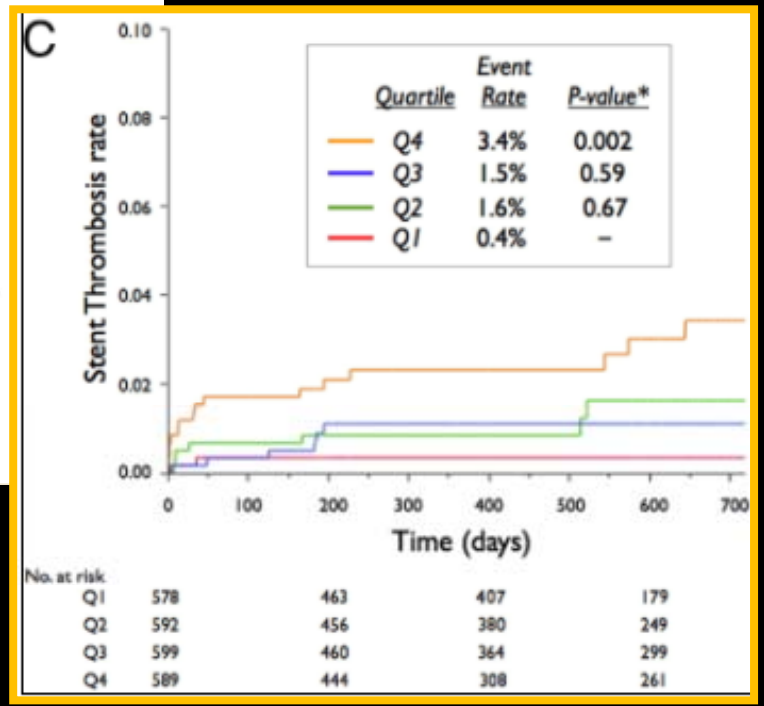
Platelet Inhibition Studies: Insight to DAPT Effectiveness

Increased Adverse Event Rates in Patients Less Responsive to Clopidogrel



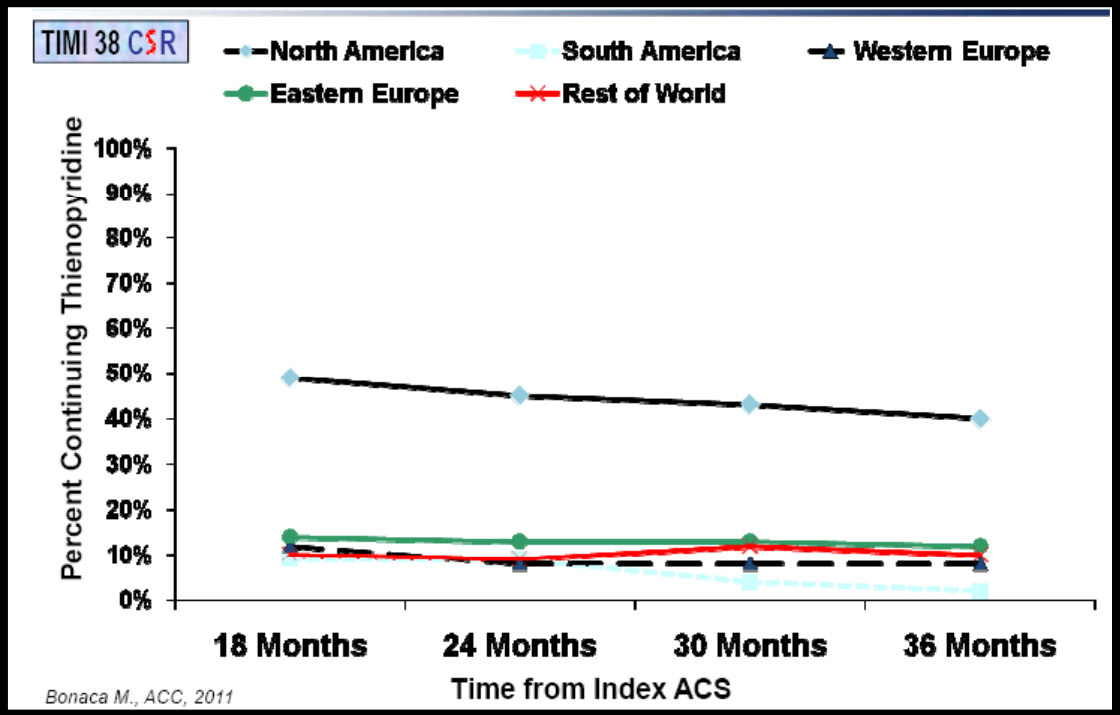
Decreased Platelet Inhibition

Clopidogrel Responsiveness
Q1: Highest Responsiveness
Q4: Lowest Responsiveness



Barr et al. JACC 2011

Patients may be prescribed DAPT longer than 12 Mo



Bonaca M., ACC, 2011

"Extending DAPT beyond 1 year is considered reasonable by some practitioners based on observational data analysis"

ACC/AHA Guidelines: Circulation 2011

"Data suggest that certain patient populations (e.g. high risk for thromboembolic events, patients after SES or PES implantation), may benefit from prolonged DAPT beyond 1 year.

ESC Guidelines: European Heart Journal 2010

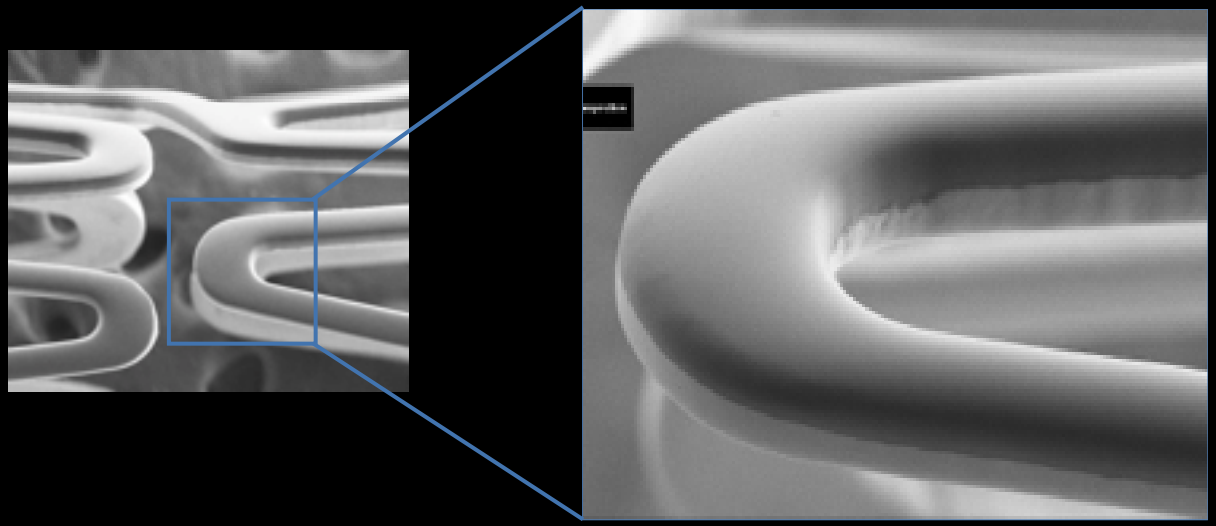
Importance of Continued DES Innovation

DAPT Considerations

DES vs. BMS	**Patient Perspective**	**Physician Perspective**
Delayed healing	Quality of life	Concerns with VLST
VLST	Side effects	Bleeding complications
Longer DAPT vs. BMS	Other therapies	Non-compliance
Discontinuation #1 ST Risk	Cost	DAPT interruption
	Peace of mind	DAPT responsiveness

SYNERGY™ Stent
Abluminal Bioabsorbable Polymer

EVOLVE



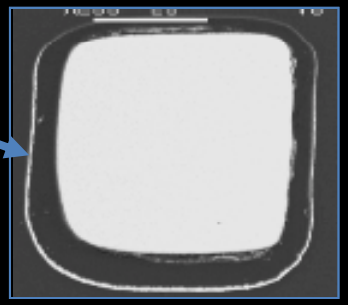
Bioabsorbable polymer (PLGA)

Applied only to the abluminal surface (rollcoat)

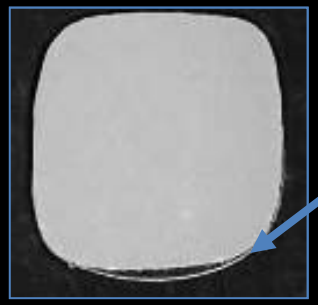
Thin strut PtCr Stent

Current Durable Polymer

Durable Permanent Polymer + Drug 360° Around Stent



Abluminal Bioabsorbable Polymer



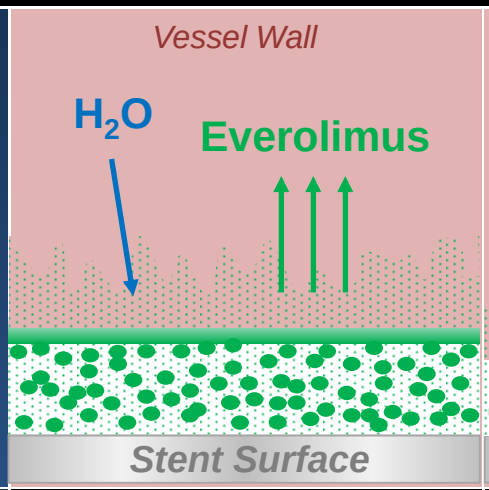
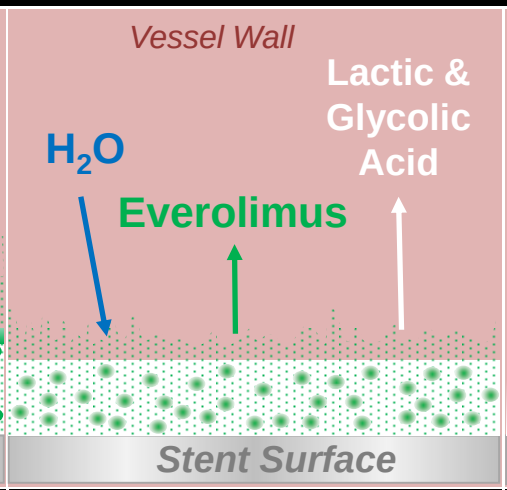
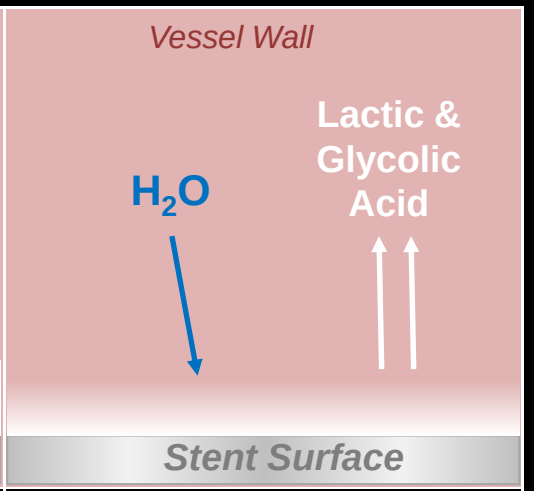
PLGA Bioabsorbable Polymer + Everolimus on Abluminal Side of Stent

Presented by Ian Meredith, MBBS, PhD at TCT 2011. The SYNERGY™ Stent is an investigational device and not for sale.

Design Goals for SYNERGY™ Stent

Drug released over 3 mo and polymer resorbed within 4 mo

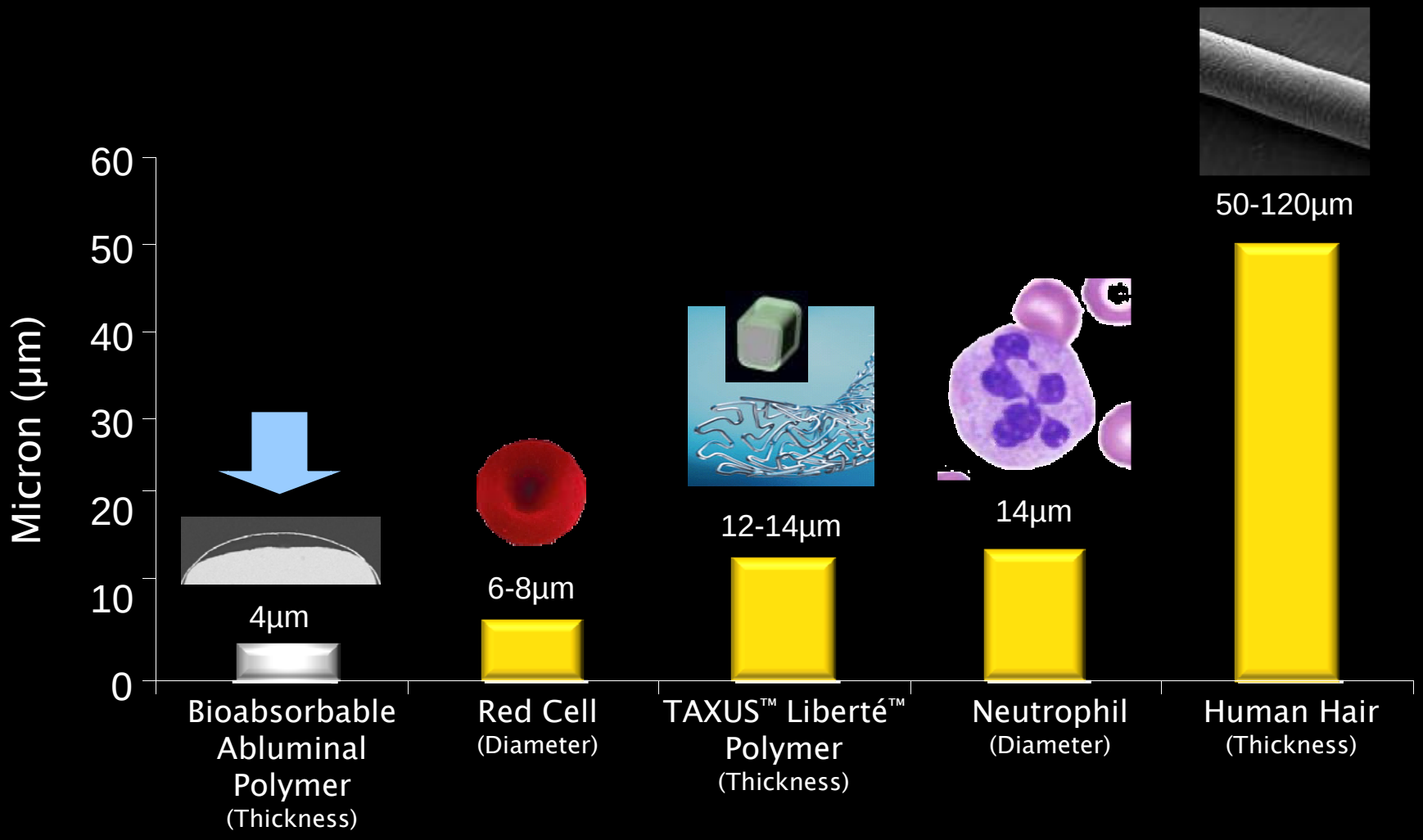
SYNERGY™ Stent

Schematic			
Drug	Burst release	Sustained release	Drug release is completed
Polymer	Hydration & polymer molecular weight reduction begins	Significant reduction in molecular weight & polymer absorption begins	Molecular weight continues to drop & remaining polymer is absorbed

BSC data on file. The SYNERGY™ stent system is an investigational device limited by law for investigational use. Not for sale.

SYNERGY™ Stent

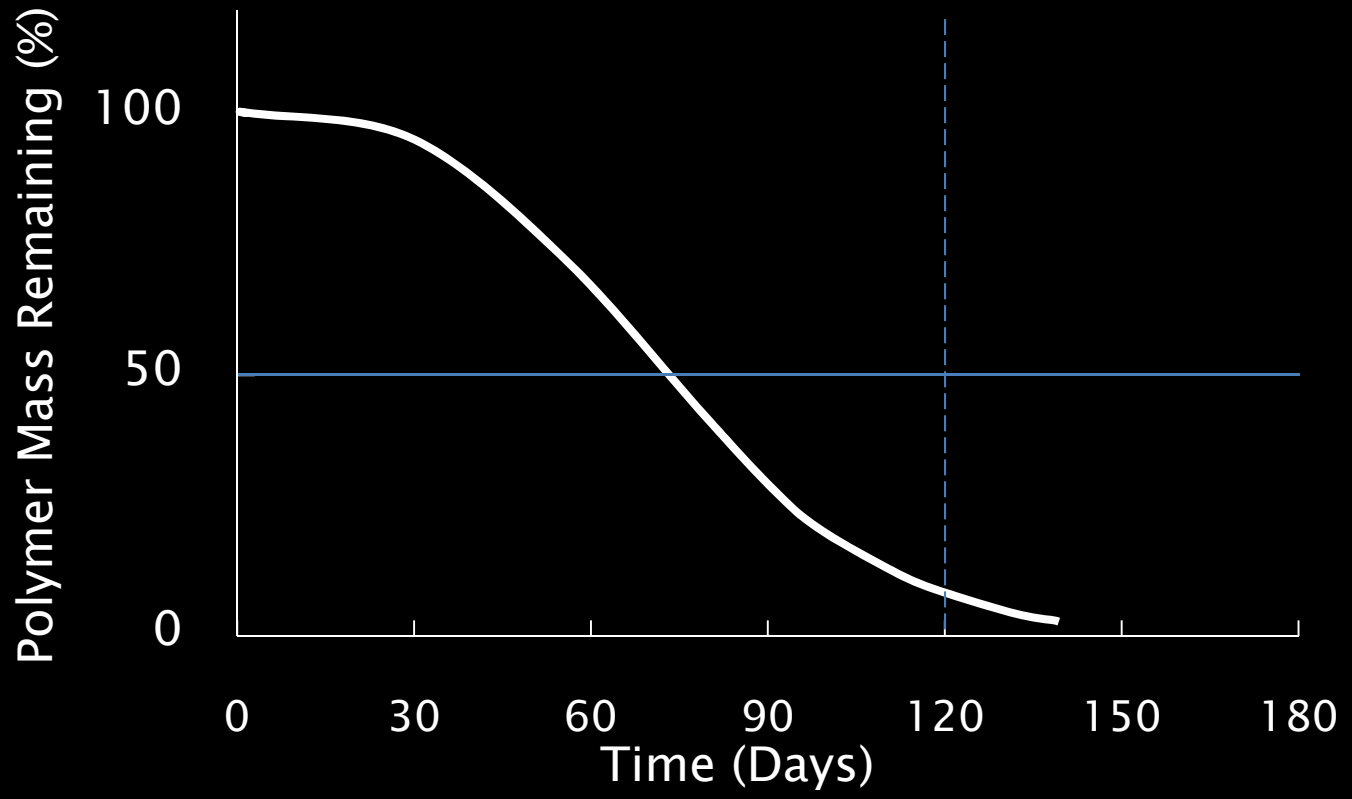
Abluminal Bioabsorbable Polymer Thickness in Perspective



The SYNERGY™ stent is an investigational device limited by law for investigational use. Not for sale.

SYNERGY™ Stent

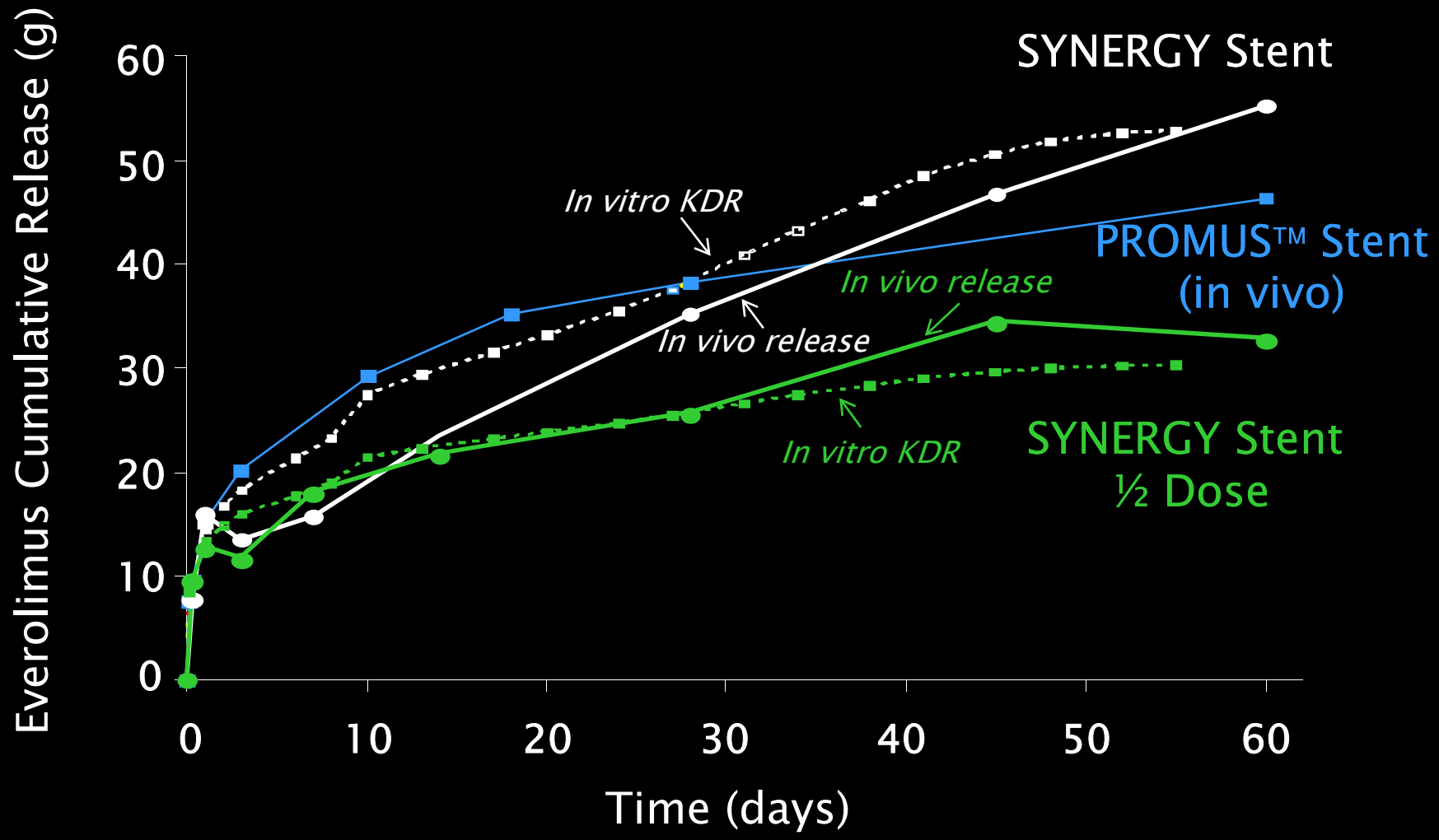
Designed for polymer resorption within 4 months



PLGA mass assessed in explanted stent and adjacent tissue

Presented by Ian Meredith AM, MBBS, PhD at TCT 2011. The SYNERGY™ stent is an investigational device limited by law for investigational use. Not for sale.

SYNERGY™ Stent Release Kinetics



Presented by Ian Meredith, MBBS, PhD at TCT 2010 • The SYNERGY stent is an investigational device. Not for sale.

SYNERGY™ Stent
Design Attributes in Perspective

Stent	Coating	Approximate Coating Thickness (μm)	Approximate Drug Load μg/mm
SYNERGY™	Abluminal	3-5	6
PROMUS™ / Xience™	Conformal	8	6
Resolute Integrity™	Conformal	6	10
BioMatrix™ Flex	Abluminal	10	16

The SYNERGY™ stent is an investigational device limited by law for investigational use. Not for sale.

EVOLVE Clinical Trials

Clinical Trial Plan for the SYNERGY™ Stent

EVOLVE FHU

291 patients

Control Device
PROMUS Element™

Primary Endpoint
30D TLF
6M Late Loss
TCT 2011

EVOLVE II

1684 patients

Control Device
PROMUS Element™ Plus

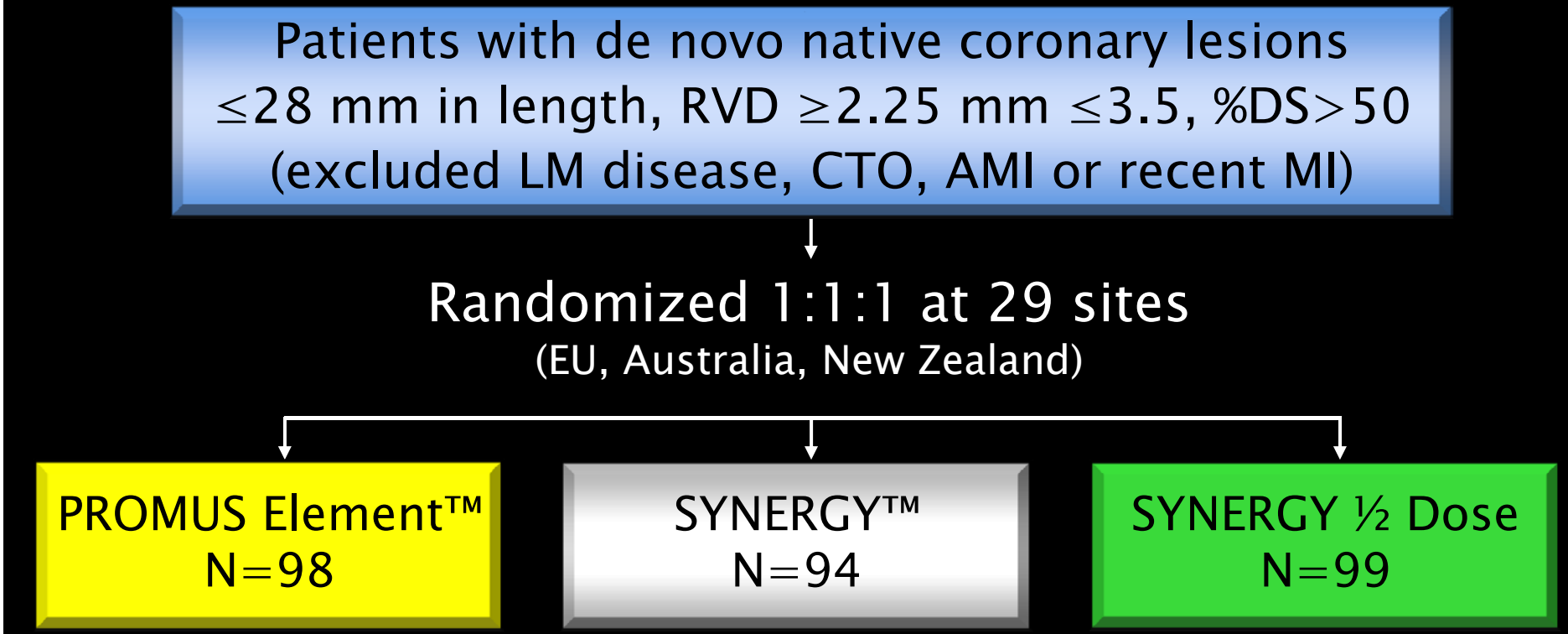
Primary Endpoint
12M TLF
2014

Planned

EVOLVE QCA/PK
EVOLVE China
EVOLVE DAPT

EVOLVE FHU: Meredith et al. *JACC* 2012. The SYNERGY™ stent is an investigational device and not for sale.

EVOLVE FHU
Study Design



Single-blind, noninferiority design

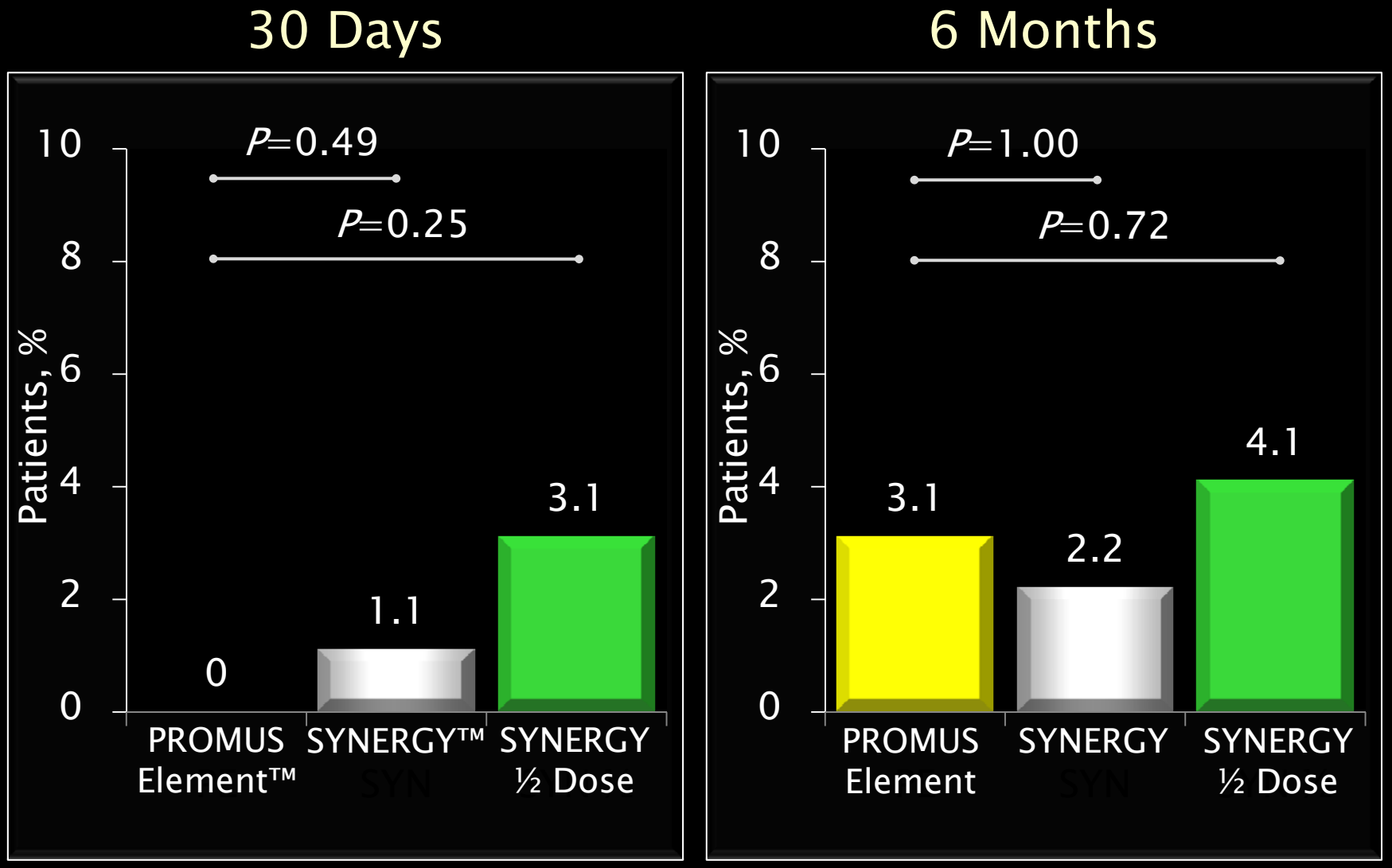
Primary Clinical Endpoint: TLF (TV-CD, TV-MI, or TLR) at 30 days

Primary Angiographic Endpoint: In-stent late loss at 6 months

Presented by Ian Meredith, MBBS, PhD at TCT 2011. The SYNERGY™ Stent is an investigational device and not for sale.

EVOLVE FHU

Target Lesion Failure



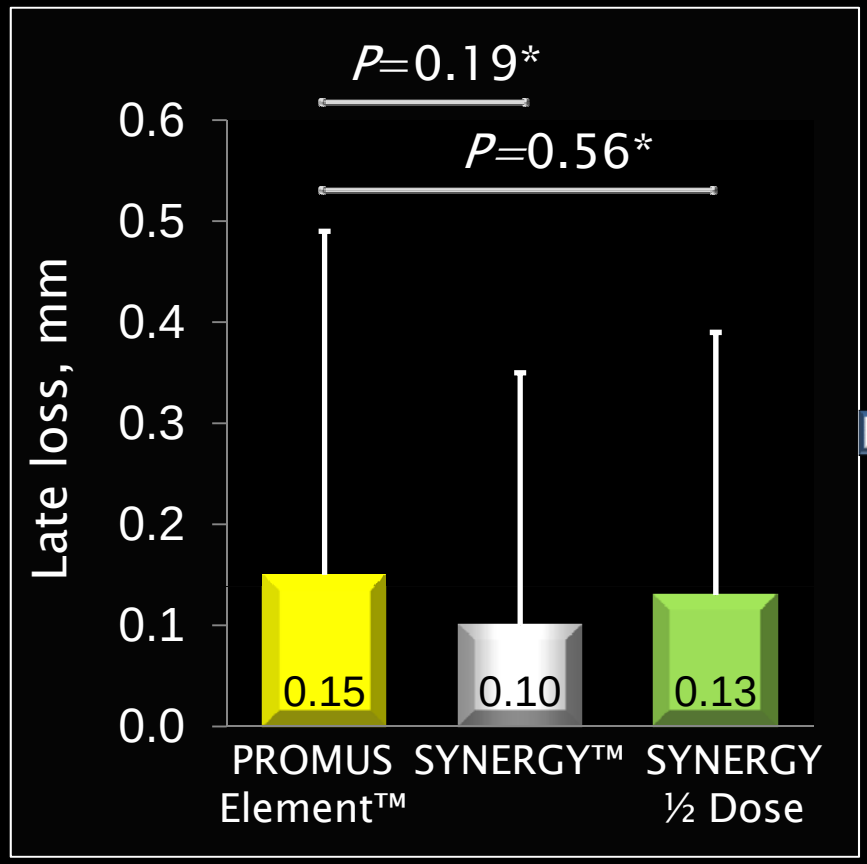
Intent-to-treat; *P* values are versus PROMUS Element (Fisher exact test)

Meredith et al. *JACC* 2012. The SYNERGY™ Stent is an investigational device and not for sale.

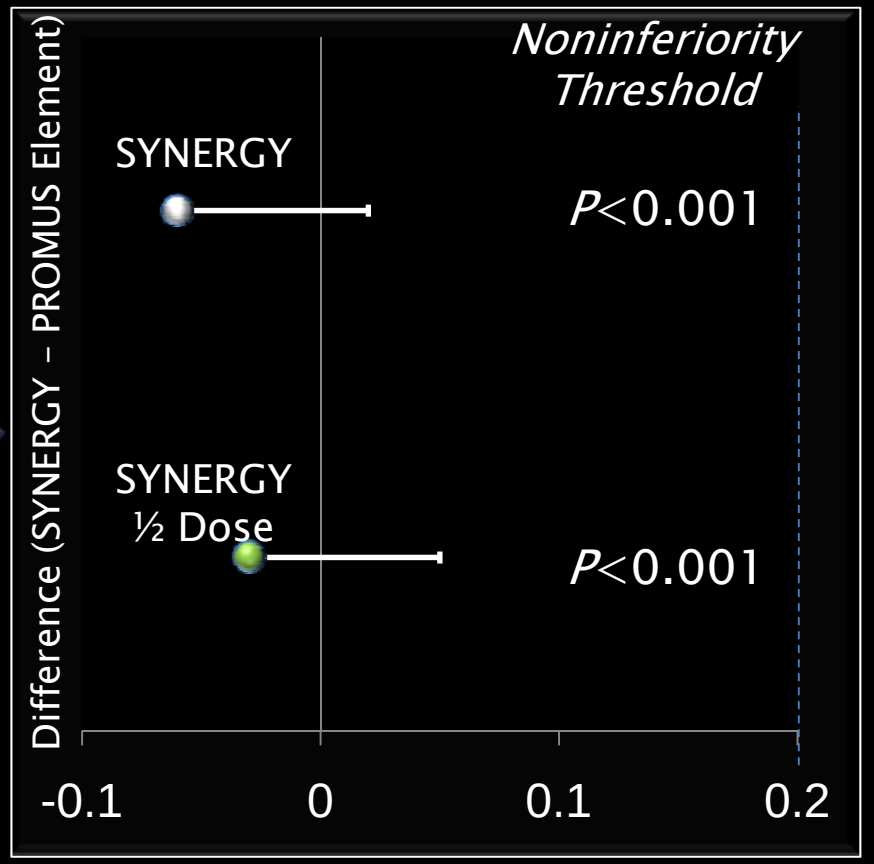
EVOLVE FHU

Late Loss at 6 Months

Late Loss at 6 Months



Difference and 95.2% UCB



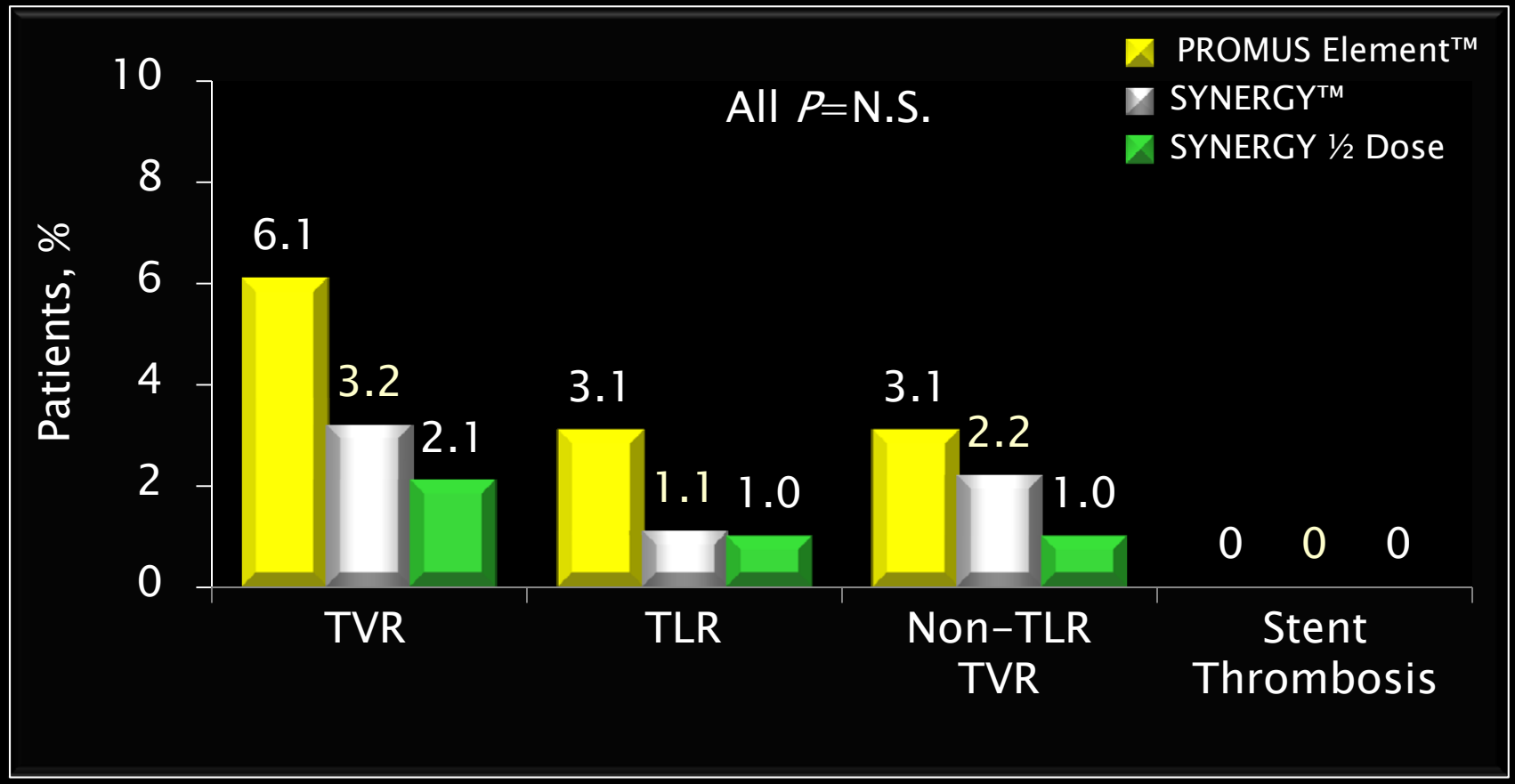
Noninferiority is proven because the upper 95.2% confidence bound of the difference in 6-month late loss is <0.20 for both SYNERGY stents

Intent-to-treat; **P* values for superiority comparison

Meredith et al. *JACC* 2012. The SYNERGY™ Stent is an investigational device and not for sale.

EVOLVE FHU

Revascularization and ST at 6 Months



Intent-to-treat; *P* values are versus PROMUS Element (Fisher exact test)

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EVOLVE II Study Design

Patients with atherosclerotic native coronary lesions
≤ 34 mm in length, RVD ≥2.25 mm ≤ 4.0, %DS ≥ 50
Up to 3 lesions in 2 vessels
(excluded LM disease, CTO, ISR, STEMI)

↓

Randomized 1:1: at up to 160 global sites

PROMUS Element™ Plus	SYNERGY™
N=842	N=842

Single-blind, noninferiority design

Primary Endpoint: TLF (CD, TV-MI, or TLR) at 12 months

Follow-up: 30 days, 6 months, 12 months, 18 months, annual 2-5 years

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Where Would the SYNERGY™ Stent Sit in the DES Landscape?

Concerns with DES

- Late ST
- DAPT Compliance
- DAPT Interruption

SYNERGY™ Stent Design

- Reduced Polymer Load
- Minimal Drug Burden
- Short Term Polymer Exposure

Desired Outcomes

- Improve late events
- Reduce DAPT duration
- Reduce risk w/DAPT interruption

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