
SYNERGY™
Everolimus-Eluting Platinum Chromium Coronary Stent System
Boston Scientific
Advancing science for life™
IN-SERVICE PRESENTATION
HEAL
WITH CONFIDENCE

Vascular Response to Current Permanent Polymers

The case for bioabsorbable polymer coatings

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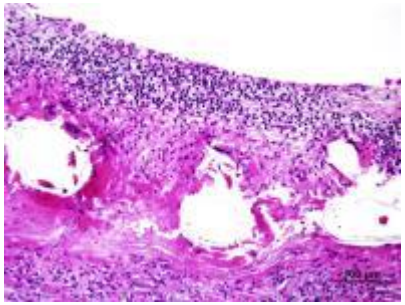
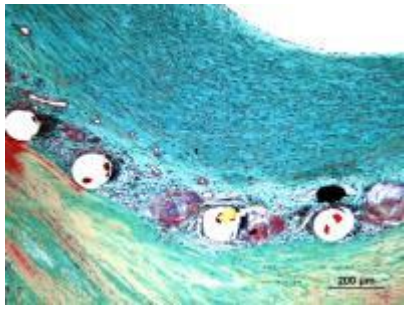
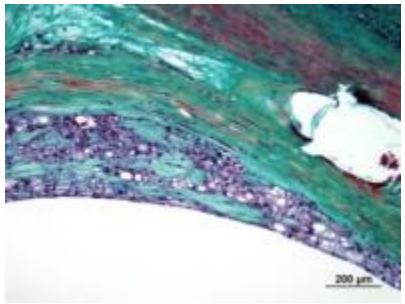
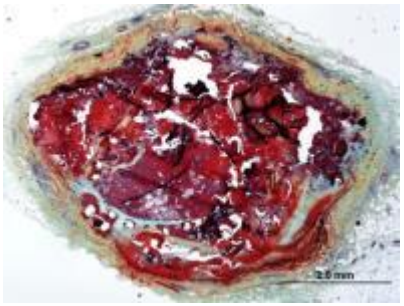
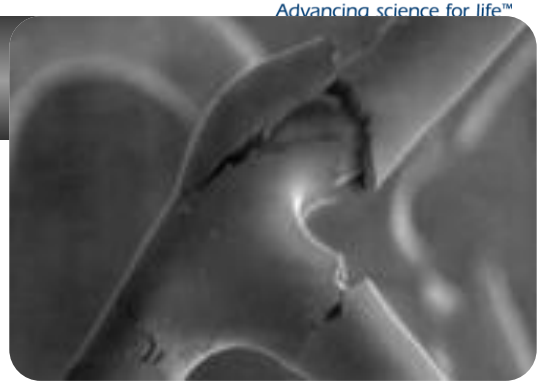
Focal Inflammation	Chronic Inflammation	Neo-Atherosclerosis	Late Stent Thrombosis
			
CoCr EES Focal inflammation with eosinophils (4 months)	CoNi ZES Chronic inflammation with giant cells secondary to polymer delamination (3 months)	CoCr EES Foamy macrophage accumulation (neoatherosclerosis)	CoCr EES EES implanted within PES (6 months antemortem)

Images Courtesy of Renu Virmani, MD.

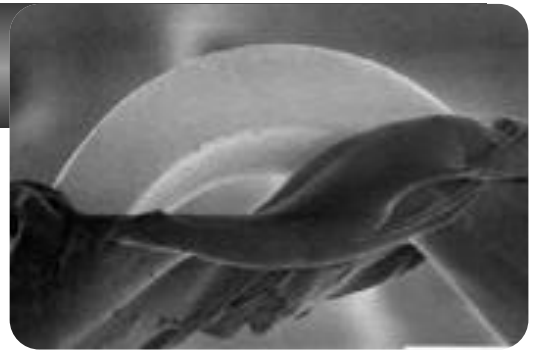
DES Polymer Considerations

What is the purpose of a DES polymer?



- Provide a mechanically stable matrix for the drug
- Modulate drug release into the vessel wall

What happens after drug release?



- Polymer remaining after drug release has no function
- All polymer coatings have the potential to be damaged
- Permanent polymers are permanent

Clinical Implications

- Late / very late events
- Chronic inflammation with neoathersclerosis
- Constant irritant may lead to late restenosis

Boston Scientific data on file.

Bioabsorbable Polymer in Perspective

Relative Polymer and Drug Absorption Profiles

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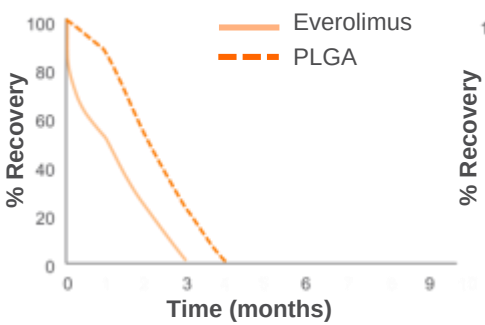
The SYNERGY Stent's polymer is absorbed shortly after drug elution ends at 3 months

Bioabsorbable Polymer-Coated Stents

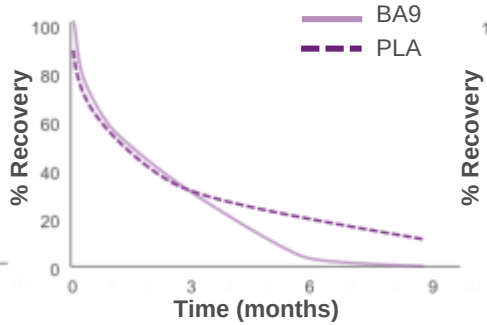
SYNERGY™[1] Stent

Polymer Coating: PLGA
Absorption Time:
3-4 mo



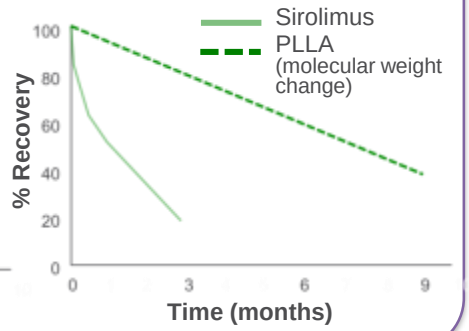
Nobori™[2] and BioMatrix Flex™[3] Stents

Polymer Coating: PLA
Absorption Time:
>9 mo



Orsiro™[4] Stent

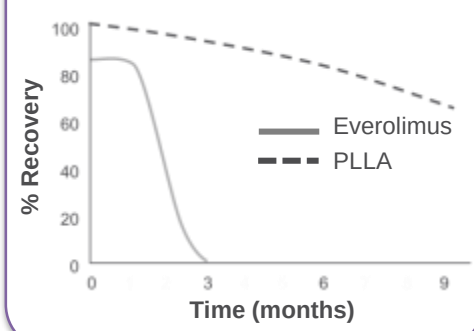
Polymer Coating: PLLA
Absorption Time:
>24 mo



Bioabsorbable Scaffold

Absorb™ BVS[3]

Polymer Scaffold: PLLA
Polymer Coating: PDLLA
Absorption Time:
>2 yrs



[1] Boston Scientific data on file. [2] *World J Cardiol* 2011 March 26; 3(3): 84-92. [3]Garg, S, *J Am Coll Cardiol*. 2010;56 (10s1):S43-S78. doi:10.1016. [4] Presented by Stephan Windecker, MD, TCT2012.

SYNERGY™ Stent

Best-in-Class Visibility

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Even with thin struts the high density of Platinum Chromium allows for greater visibility*

	SYNERGY Stent	Promus PREMIER™ Stent	Resolute Integrity™ Stent	XIENCE Xpedition™ / Alpine™ Stent
Alloy	PtCr	PtCr	CoNi	CoCr
Strut Thickness	74 µm**	81 µm	91 µm	81 µm

*Testing Completed by Boston Scientific data on file. 2.5 mm stent products tested. Based on 2.5mm stents. Under 6.0mm copper phantom to simulate body mass. Bench test results may not necessarily be indicative of clinical performance.
**Strut thickness for small vessel model is 74µm, Workhorse model is 79µm and large vessel is 81µm. Boston Scientific data on file.

SYNERGY™ Stent

Product Summary

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Thin Struts and Lower Coating Thickness

	SYNERGY[1] Stent	Xience V™, Xience Prime™[1], Xience Xpedition™[1], Xience Alpine™ Stents PROMUS Element™[1] Stent Promus PREMIER™ Stent	BioMatrix Flex™[2] Stent	ABSORB™ BVS[3]
				
Strut Thickness	74 µm* (0.0029”)	81 µm (0.0032”)	120 µm (0.0047”)	150 µm (0.0059”)
Polymer Coating Type & Thickness	Bioabsorbable Abluminal 4 µm	Conformal Permanent 8 µm	Bioabsorbable Abluminal 10 µm	Bioabsorbable Conformal 3 µm / side
Total Coated Strut Thickness	78 µm	97 µm	130 µm	156 µm

*Strut thickness for small vessel model is 74µm, Workhorse model is 79µm and large vessel is 81µm. Boston Scientific data on file. Representative drawings are to scale. Representative drawings. 1 Wilson GW, EuroIntervention 2012;8:250-257, and Soucy NV, EuroIntervention 2010;6:630-637. 2 Gutiérrez-Chico JL, American Heart Journal November 2011; 162:922–931. 3 Onuma Y, Circulation 2011, 123:779-797. Bench test results may not necessarily be indicative of clinical performance.

SYNERGY™ Stent

1 month DAPT labelling update now CE marked

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Individualisation of Patient Treatment

The device carries an associated risk of acute, sub-acute or late thrombosis, vascular complications, and/or bleeding events. Therefore, patients should be carefully selected, and a $P2Y_{12}$ inhibitor (i.e., clopidogrel, ticlopidine, prasugrel, or ticagrelor) must be prescribed post procedure to reduce the risk of stent thrombosis. Aspirin must be administered concomitantly with the $P2Y_{12}$ inhibitor, and then continued indefinitely to further reduce the risk of thrombosis.

Antiplatelet drugs should be used in combination with SYNERGY which is designed with a low initial polymer load, abluminal coating and bioabsorbable polymer which may reduce the risk of thrombosis and the need for prolonger dual antiplatelet therapy.

Physicians should use the information from the large body of clinical evidence for everolimus drug eluting stents, coupled with current literature on drug-eluting stents, current European Society of cardiology recommendation or other applicable country guidelines and the specific needs of the individual patient to determine the specific antiplatelet / anticoagulation regimen to be used for their patients in general practice.

It is very important that the patient be compliant with post-procedural antiplatelet recommendations given by their physician. In selected higher risk patients where the physician determines that the risks outweigh the benefits of continued DAPT, it may be reasonable to interrupt or discontinue therapy after 1 month based on low stent thrombosis rates and no observed increased risk for stent thrombosis as shown in the current literature. Patients who require premature discontinuation of antiplatelet therapy should be monitored closely and have their antiplatelet therapy restarted as soon as possible per the discretion of their treating physician.

^ The updated Directions for Use will also include an update on the current "Pre-and Post-Procedure Antiplatelet Regimen":
In selected higher risk patients where the physician determines that the risks outweigh the benefits of continued DAPT, it may be reasonable to interrupt or discontinue therapy after 1 month based on low stent thrombosis rates and no observed increased risk for stent thrombosis as shown in the current literature. Patients who require premature discontinuation of antiplatelet therapy should be monitored closely and have their antiplatelet therapy restarted as soon as possible per the discretion of their treating physicians

SYNERGY™ Coronary Stent System

New Indications and Labelling Updates Now CE Marked

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CE Mark	
✓	Acute Coronary Syndrome (ACS)
✓	Acute Myocardial Infarction (AMI)
✓	Unstable Angina
✓	Renal Failure
✓	Coronary Bifurcation Lesions[1]
✓	Coronary Multi-vessel Disease
✓	Coronary Saphenous Vein Graft Lesions
✓	Coronary Artery Ostial Lesions
✓	Unprotected Left Main Coronary Artery Lesions
✓	Coronary Artery Total Occlusion Lesions[2]
✓	In-Stent Restenosis in Coronary Artery Lesions[3]

[1] When treating Bifurcations, care must be exercised to access the secondary vessel via the repeating geometry in the body of the stent within the primary vessel.
[2] For treatment of occluded vessels, contrast visualization of the distal vessel to confirm position of guidewire within the lumen is recommended.
[3] For in stent restenosis, where details of the original stent are known, the expanded inner diameter of the new stent should not exceed the dilation limits of the original stent. Where details of the original stent are not known, the expanded inner diameter of the new stent should not exceed the reference vessel diameter.

Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device. Information for the use only in countries with applicable health authority product registrations.

SYNERGY™ Stenting Left Main

SYNERGY™ Stent is indicated for treatment of patients presenting with unprotected left main coronary artery lesions:

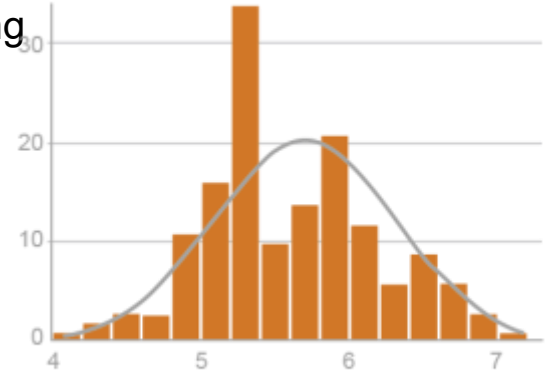
LM
Left Main Stenting

- **Left Main vessels are Large (>5.5mm on average[1])**
- SYNERGY™ Stent is indicated for treatment of patients presenting with unprotected left main coronary artery lesions
- SYNERGY has a labeled overexpansion indication of up to 5.75mm[2]

- **Left Main Vessels require stents with significant radial strength[3]**
- SYNERGY offers excellent radial strength[4]

- **Left Main PCI needs optimal Vessel Healing[3]**
- The SYNERGY DES shows healing within 3-month and has low risk of cardiac adverse events in complex patients[5]

IVUS LM in male patients



Graph Prof. Robert Jan van Geuns. IVUS LM in male pts (Rotterdam). Asia PCR 2015.
IVUS data on 865 LAD->LM pullbacks, male patients . Average Vessel Diameter (VD): 5.60 mm , Mean VD: 5.47 mm. Only in 13% <5 mm.

1. Shand J, et al. Prospective Intravascular Ultrasound Investigation of the Necessity for and Efficacy of Postdilation Beyond Nominal Diameter of 3 Current Generation DES Platforms for the Percutaneous Treatment of the Left Main Coronary Artery. Cathet Cardiovasc Intv; 2014;84:351-358.
2. Labeled Post-Dilatation Limits. SYNERGY Stent, Xience Xpedition Stent , Resolute Integrity Stent and Resolute Onyx DFU
3. Adapted from presentations by Prof. RJ van Geuns, MD, PhD; and Jiang Ming Fam, MD at AsiaPCR 2015
4. Bench testing performed by Boston Scientific Corporation. Data on file at Boston Scientific. All stents 2.5mm. SYNERGY Stent n=5, all other stents are n=3. Bench test results not necessarily indicative of clinical performance.
5. EVOLVE Clinical trial at 4 year. Presented by Ian T. Meredith AM, MBBS, PhD, PCR 2015. EVOLVE II Clinical Trial. Presented by Dean J. Kereiakes, MD at AHA 2014. EVOLVE II DM Clinical Trial. Presented by Stephan Windecker, MD at PCR 2015. Adapted from a presentation by J. M. de la Torre, MD at PCR 2015. Wilson G, MD. ACC 2011.

SYNERGY™ Stenting Total Occlusion

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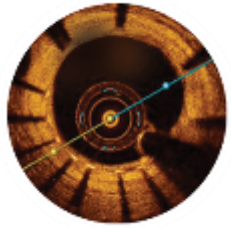
SYNERGY™ Stent is indicated for treatment of patients presenting with total occlusion coronary artery lesions:

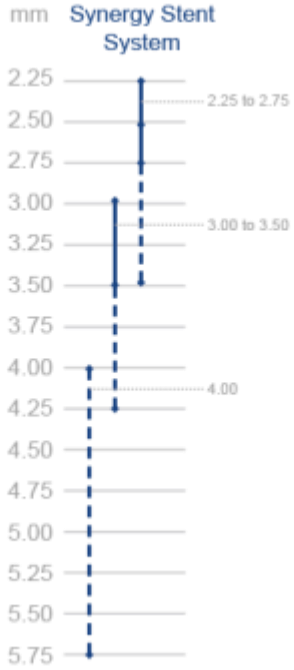
CTO
Chronic Total Occlusion

- **CTO lesions tend to be long and located in large vessels**
- SYNERGY has a labeled **overexpansion** of **up to 5.75mm**, allowing the physician to customize the stent to the appropriate vessel size[1]

- **Stent mechanical properties are important considerations for CTO stenting**
- The SYNERGY Stent's customized architecture offers exceptional **strength** and **conformability**[2]

- The SYNERGY DES shows **healing within 3-months** and has low risk of cardiac adverse events **in complex patients**[3]





For treatment of occluded vessels with the SYNERGY stent system, contrast visualization of the distal vessel to confirm position of guidewire within the lumen is recommended.

1 Labeled Post-Dilatation Limits. SYNERGY Stent, Xience Xpedition Stent , Resolute Integrity Stent and Resolute Onyx DFU

2 Bench testing performed by Boston Scientific Corporation. Data on file at Boston Scientific. All stents 2.5mm. SYNERGY Stent n=5, all other stents are n=3. Bench test results not necessarily indicative of clinical performance.

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SYNERGY™ Stenting Bifurcation

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SYNERGY™ Stent is indicated for treatment of patients presenting with bifurcation coronary artery disease:

BIF
Bifurcation Lesions

- **Bifurcation lesions are often tapered**[1]
- SYNERGY has a labeled **overexpansion** of **up to 5.75mm**, allowing the physician to customize the stent to the appropriate vessel size and ensure great apposition[2]
- **With bifurcation we want to maintain the natural vessel shape**[1]
- The SYNERGY Stent's customized architecture offers exceptional **strength** and **conformability**[3]
- **Bifurcation PCI benefits from an appropriate Cell Diameter & Expansion**[1]
- The SYNERGY Stent has **large cell diameters** in the body of the stent to accommodate side branch access[4]
- **Bifurcation lesions need optimal Vessel Healing to reduce risk of ST**[1]
- The SYNERGY DES shows **healing within 3-month** and has low risk of cardiac adverse events **in complex patients**[5]

When treating Bifurcations, care must be exercised to access the secondary vessel via the repeating geometry in the body of the stent within the primary vessel.

1 Attributes collected from: Curtiss T. Stinis, M.D., F.A.C.C, F.S.C.A.I. - Scripps CI 2013 and ESC/EACTS GUIDELINES 2014. EHJ doi:10.1093/eurheartj/ehu278. 2 Labeled Post-Dilatation Limits. SYNERGY Stent, Xience Xpedition Stent , Resolute Integrity Stent and Resolute Onyx DFU 3 Bench testing performed by Boston Scientific Corporation. Data on file at Boston Scientific. All stents 2.5mm. SYNERGY Stent n=5, all other stents are n=3. Bench test results not necessarily indicative of clinical performance. 4 Circular Cell Diameter: n = 5. Data on file at Boston Scientific. Size Matrix on the SYNERGY Stent DFUs. 5 EVOLVE Clinical trial at 4 year. Presented by Ian T. Meredith AM, MBBS, PhD, PCR 2015. EVOLVE II Clinical Trial. Presented by Dean J. Kereiakes, MD at AHA 2014. EVOLVE II DM Clinical Trial. Presented by Stephan Windecker, MD at PCR 2015. Adapted from a presentation by J. M. de la Torre, MD at PCR 2015. Wilson G, MD. ACC 2011.

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SYNERGY™ Stent System

Improved Design for Superior Deliverability

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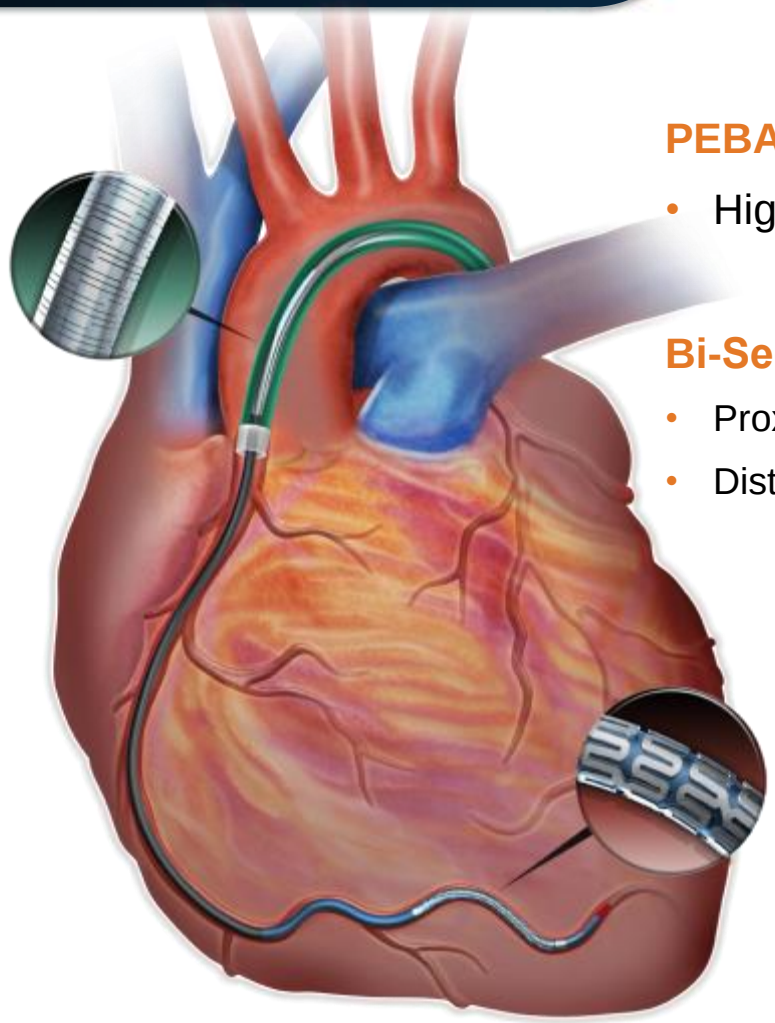
NEW Laser-Cut Hypotube

- ~300 cuts over 100 mm length
- Extends into midshaft to exit port to improve pushability
- Additional length maintains midshaft flexibility
- ↑ Pushability and Flexibility



PEBAX Dual-Layer Balloon

- Highly flexible

Bi-Segment™ Inner Lumen

- Proximal segment for push
- Distal segment for flexibility

The graphic design does not represent actual vessel anatomy nor the actual size of the SYNERGY device. Data on file at Boston Scientific.

SYNERGY™ Stent System

*Labeled Post-Dilatation Limits**

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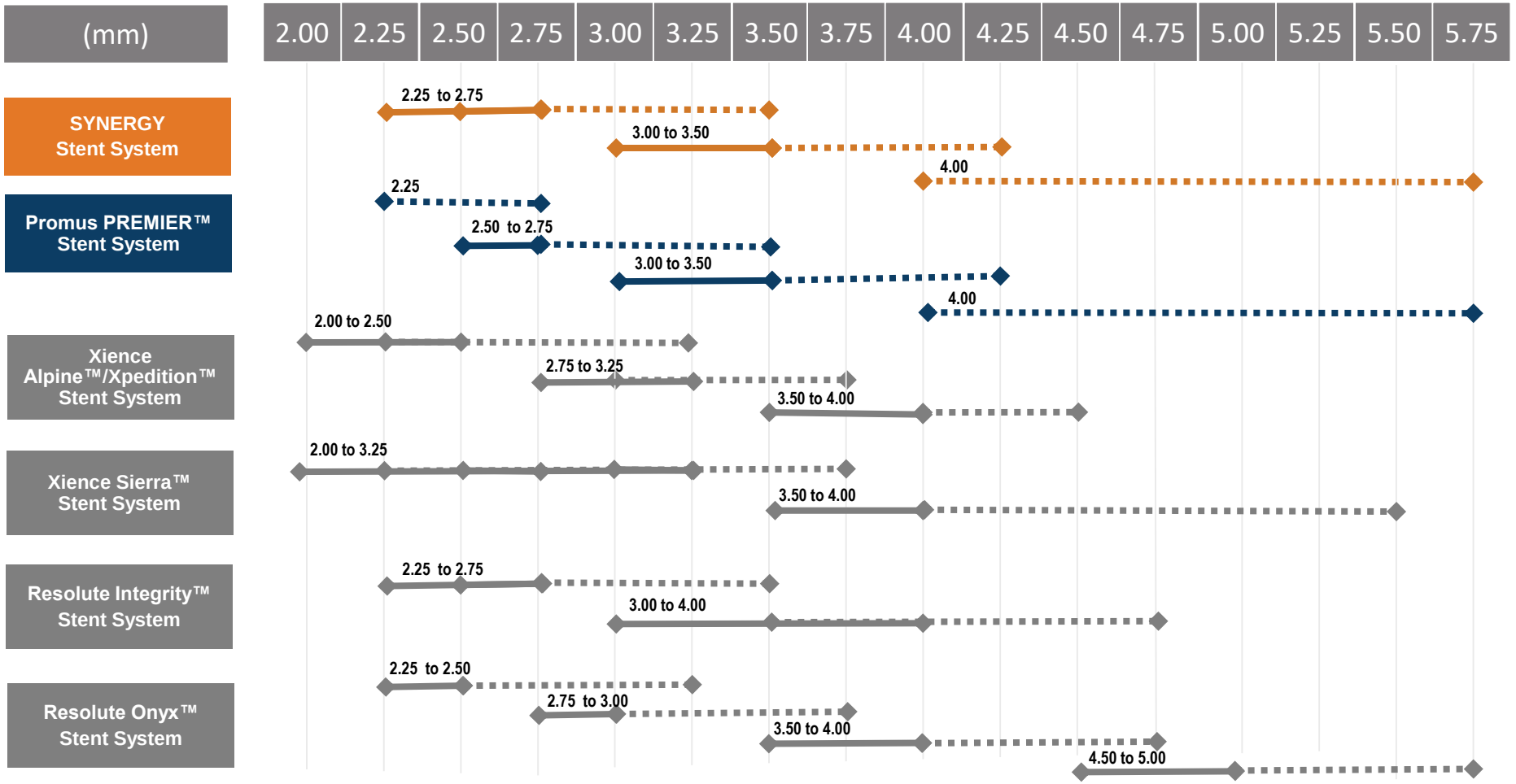

*SYNERGY Stent, Promus PREMIER Stent, Xience Xpedition Stent, Xience Alpine Stent, Xience Sierra Stent, Resolute Integrity Stent and Resolute Onyx DFU.

SYNERGY and PREMIER 4.0mm dedicated stent, with 1.75mm overexpansion capability, is more versatile when sizing for the LAD and LCX and over-expanding to fit the LM

Kang Network Meta-Analysis:
Relative ST risk at 1-year from 111,088 patients

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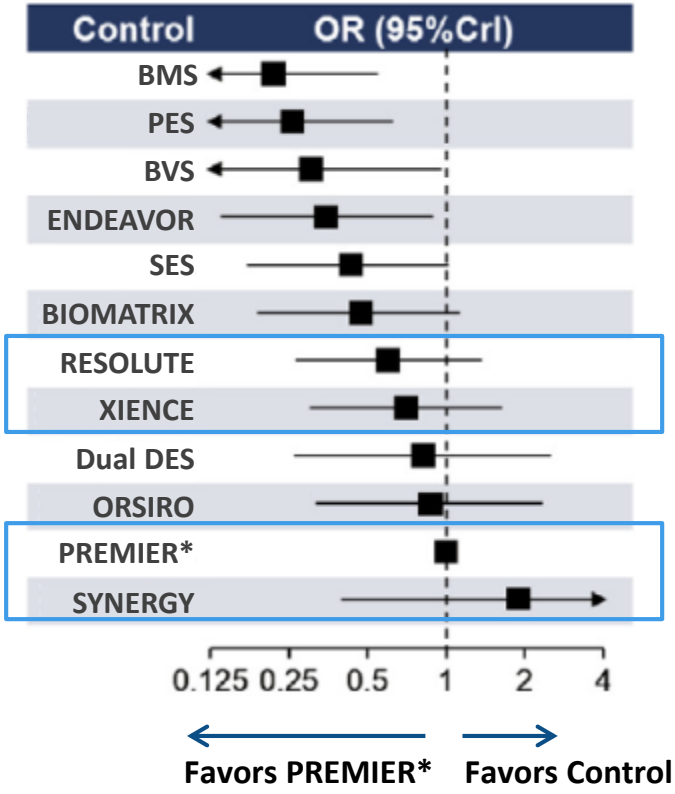
SYNERGY ™ BP Stent Ranked #1 and Promus PREMIER ™ PP Stent Ranked #2 for the lowest relative risk of Definite/Probably Stent Thrombosis

Promus PREMIER vs. comparators



STUDY DESIGN (ST Analysis)

- 110 prospective, randomized controlled trials included
- 111,088 patients
- Primary endpoint: definite or probable stent thrombosis at 1 year

Caution should be taken in interpreting study results, as some stents had limited numbers of comparisons, and some of the studies had a potential risk of bias. *All PtCr-EES stents, also includes PROMUS Element and PROMUS Element Plus. Def/prob ST was available in 110 studies with 111,088 patients.
Kang, S.et al. J Am Coll Cardiol Intv. doi:10.1016/j.jcin.2016.03.038

SYNERGY™ Stent System

Summary

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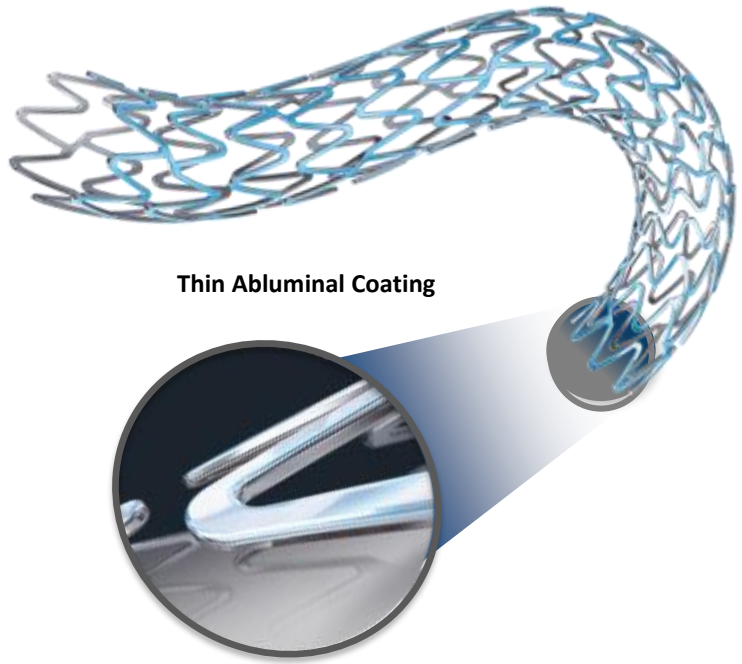
Providing operational efficiency, optimal[1] healing, and freedom from long-term polymer exposure

- SYNERGY™ Stent offers **peace of mind** knowing that the polymer is gone shortly after the drug is completely eluted at 3 months[2]
- SYNERGY Stent has **shown full stent strut coverage** as early as 30-days in humans and showed 0% stent thrombosis in multiple OCT analyses.[3]
- **Unmatched acute performance** which reduces procedure time as much as 5 minutes per case.[4]



[1] Eppihimer M, PhD. Impact of Polymer Type and Location on Stent Thrombogenicity and Endothelial Cell Coverage. EuroPCR 2014.
[2] Wilson, G.J., et al. *Catheter Cardiovasc Interv*. 2015.
[3] OCT Analyses: SORT OUT VIII - Adapted from presentation by Ida Riise Balleby, MD at PCR 2015; OCT Analysis presented by J. M. de la Torre, MD at TCT 2014; TIMELESS - Adapted from presentation by Juan Granada, MD, at CRT 2015; Burgos-Santander Study - Adapted from a presentation by J. M. de la Torre, MD at PCR 2015.
[4] US IC Blinded Product Perception survey (62 ICs), Increased stent visibility was estimated to decrease stent usage by 14% balloon usage by 18% during a typical PCI and 5 minutes less procedure time in IC Perception survey; 95% (59/62) identified
the PtCr stent as the most visible.