

Boston Scientific

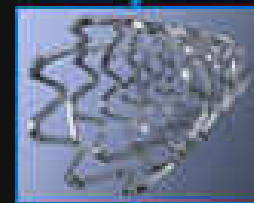
DES Current & Future Perspectives

Keith Dawkins MD FRCP FACC FSCAI
Associate Chief Medical Officer
Senior Vice President
Boston Scientific Corporation

Summit TCT Asia Pacific 2009

April 22-24, 2009

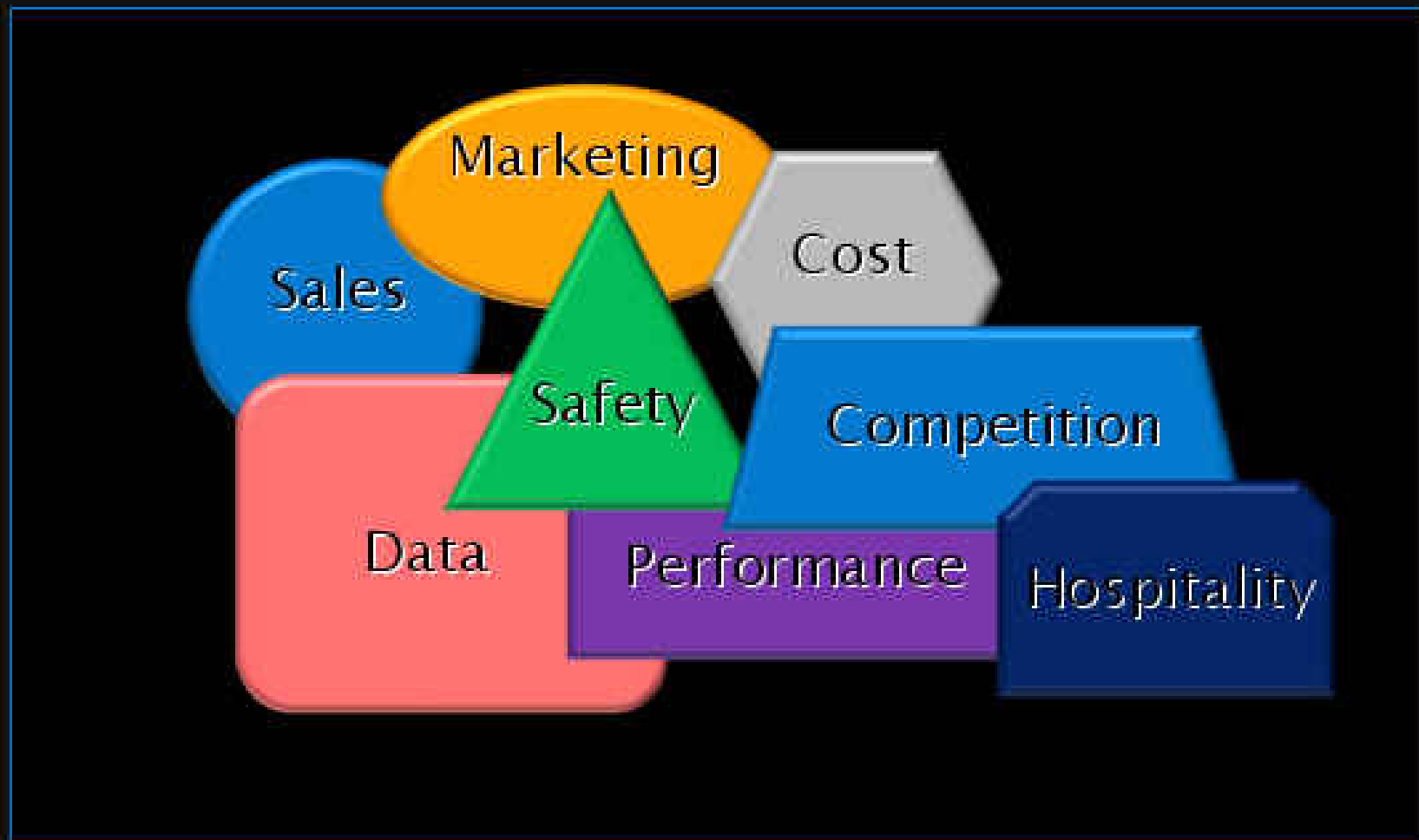
The Convention Center of Sheraton Grand (Marriott Hotel), Seoul, Korea



Conflicts of Interest

- **Employee**
 - Boston Scientific Corporation
- **Stockholder**
 - Boston Scientific Corporation

Why do ICs buy a particular Stent?



Boston Scientific Two-Drug Strategy

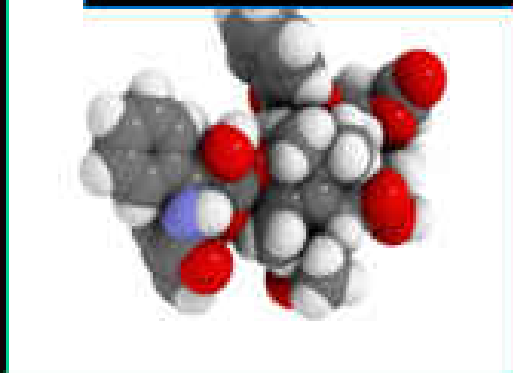
TAXUS Liberté



PROMUS



Why does BSC persist with the Two-Drug Strategy?

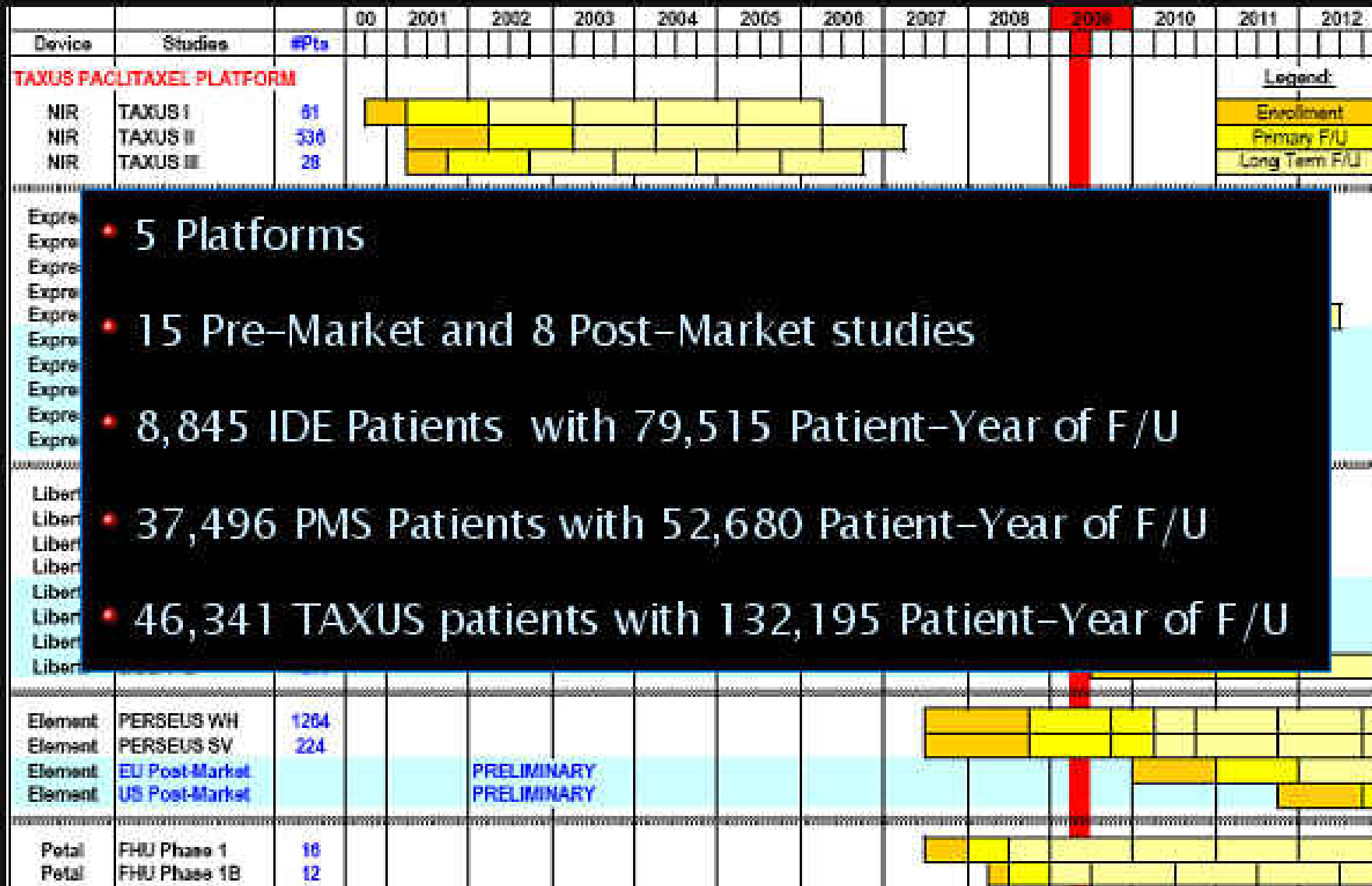


October 10th 2008



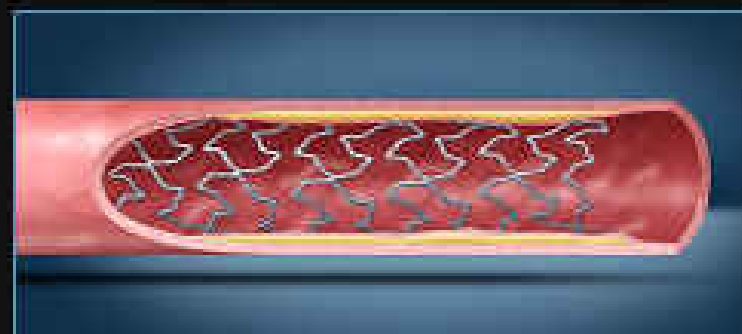
July 2nd 2008

The TAXUS Program

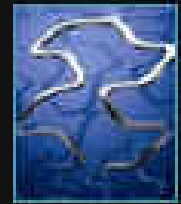


- 5 Platforms
- 15 Pre-Market and 8 Post-Market studies
- 8,845 IDE Patients with 79,515 Patient-Year of F/U
- 37,496 PMS Patients with 52,680 Patient-Year of F/U
- 46,341 TAXUS patients with 132,195 Patient-Year of F/U

TAXUS[®] Liberté[®]
Paclitaxel-Eluting
Coronary Stent
System



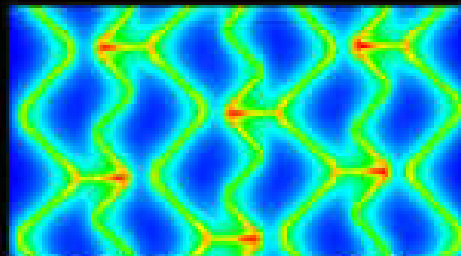
TAXUS[®] Liberté[®] Paclitaxel-Eluting Coronary Stent System



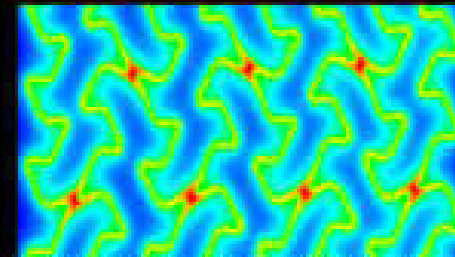
Hybrid Cell Design



Uniform Cell Geometry



TAXUS[®] Express[®] Stent



TAXUS[®] Liberté[®] Stent

Crossing Profile

T. Express[®] Stent





0.049''

T. Liberté[®] Stent



0.047''

Stent Platforms: Strut & Polymer Thickness*

	TAXUS Express ²	TAXUS Liberté
Stent Material	316L Stainless Steel	
Stent Pattern		
Strut Thickness	0.0052"	0.0038"
Strut Width	.0028/.0036"	.0030"
Drug Density	1.0 µg PTx/mm ² stent surface	
Drug Dose (µg) [†]	108	77

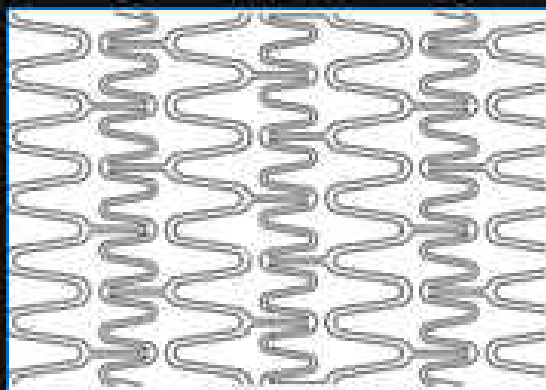
[†]2.25x16mm Stent

TAXUS Stent Design

TAXUS Express²

Diam: 2.25 - 5.0mm

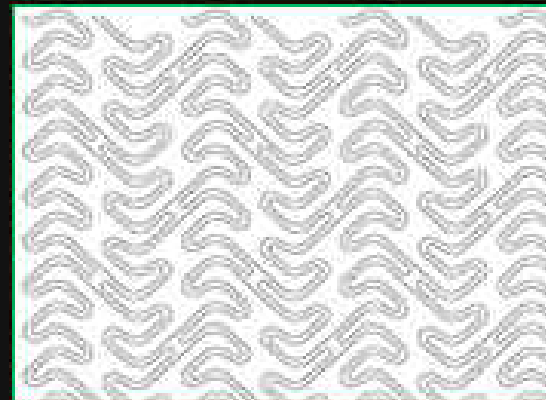
Stent Designs: 2
(WH + LV)



TAXUS Liberté

Diam: 2.25 - 5.0mm

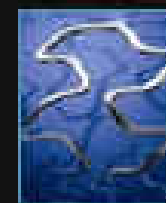
Stent Designs: 3
(SV + WH + LV)



Allows for more consistent performance across diameter range

TAXUS[®] ATLAS Trial Series

Evaluating the TAXUS[®] Liberté[®] Stent



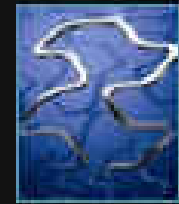
	Initial PMA Approval			
Liberté Stent Patients	ATLAS DE NOVO N=871	ATLAS LONG N=150	ATLAS SMALL N=261	ATLAS DIRECT N=247
9m 1 ^o Endpoint	9 Month TVR	9 Month % Diameter Stenosis (Analysis Segment)		
Case-matched Control	TAXUS [®] Express [®] Stent from TAXUS IV & V	TAXUS Express Stent from TAXUS IV & V	TAXUS Express Stent from TAXUS V	TAXUS Liberté Stent from TAXUS ATLAS
RVD	2.5 - 4.0 mm	2.7 - 4.0 mm	2.2 - 2.5 mm	2.5 - 4.0 mm
Lesion Length	10 - 28 mm	26 - 34 mm	10 - 28 mm	10 - 28 mm
Multiple Stenting	No			

TAXUS
ATLAS Pooled Data

In the ATLAS Trial, the primary end point (9m TVR) was met, demonstrating that TAXUS Liberté is non-inferior to the TAXUS Express² Stent.

[J Am Coll Cardiol. 2007;49:1676-1683](#)

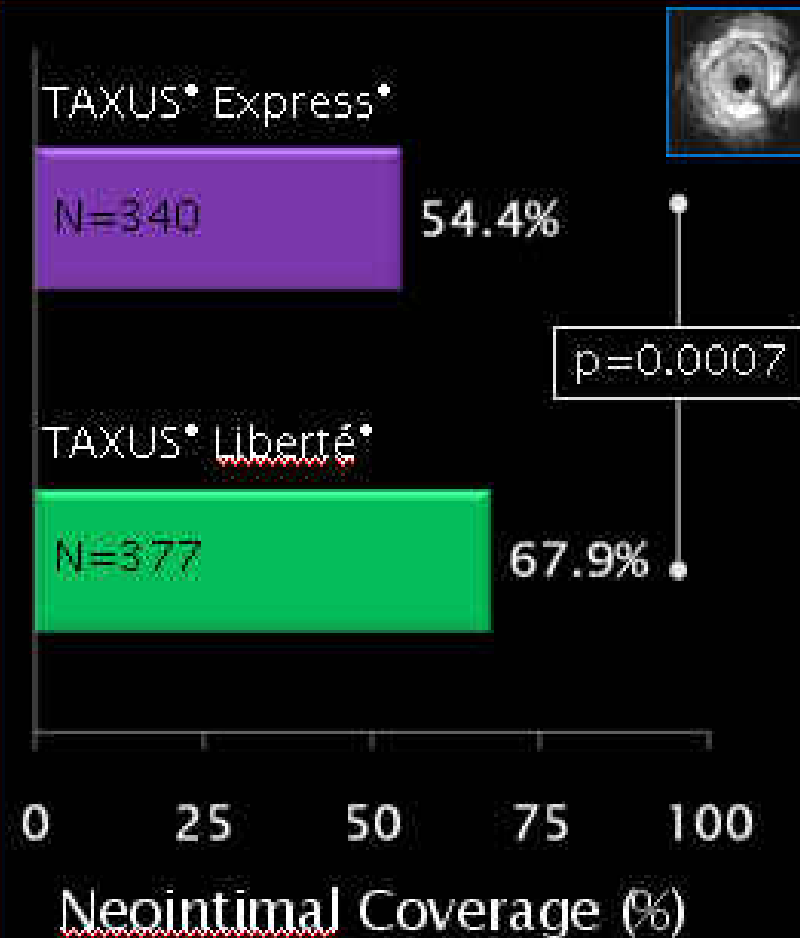
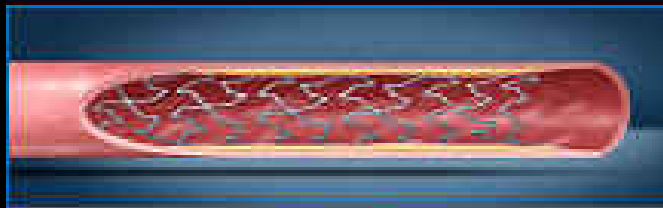
TAXUS[®] ATLAS IVUS Analysis



TAXUS[®] Liberté[®] Stent:

- Increased Neointimal Coverage ($p=0.0007$)
- Similar In-Stent Net Volume Obstruction (%) ($p=0.56$)
- Less Late Incomplete Stent Apposition ($p=0.0385$)

*...compared with the
TAXUS[®] Express[®] Stent*



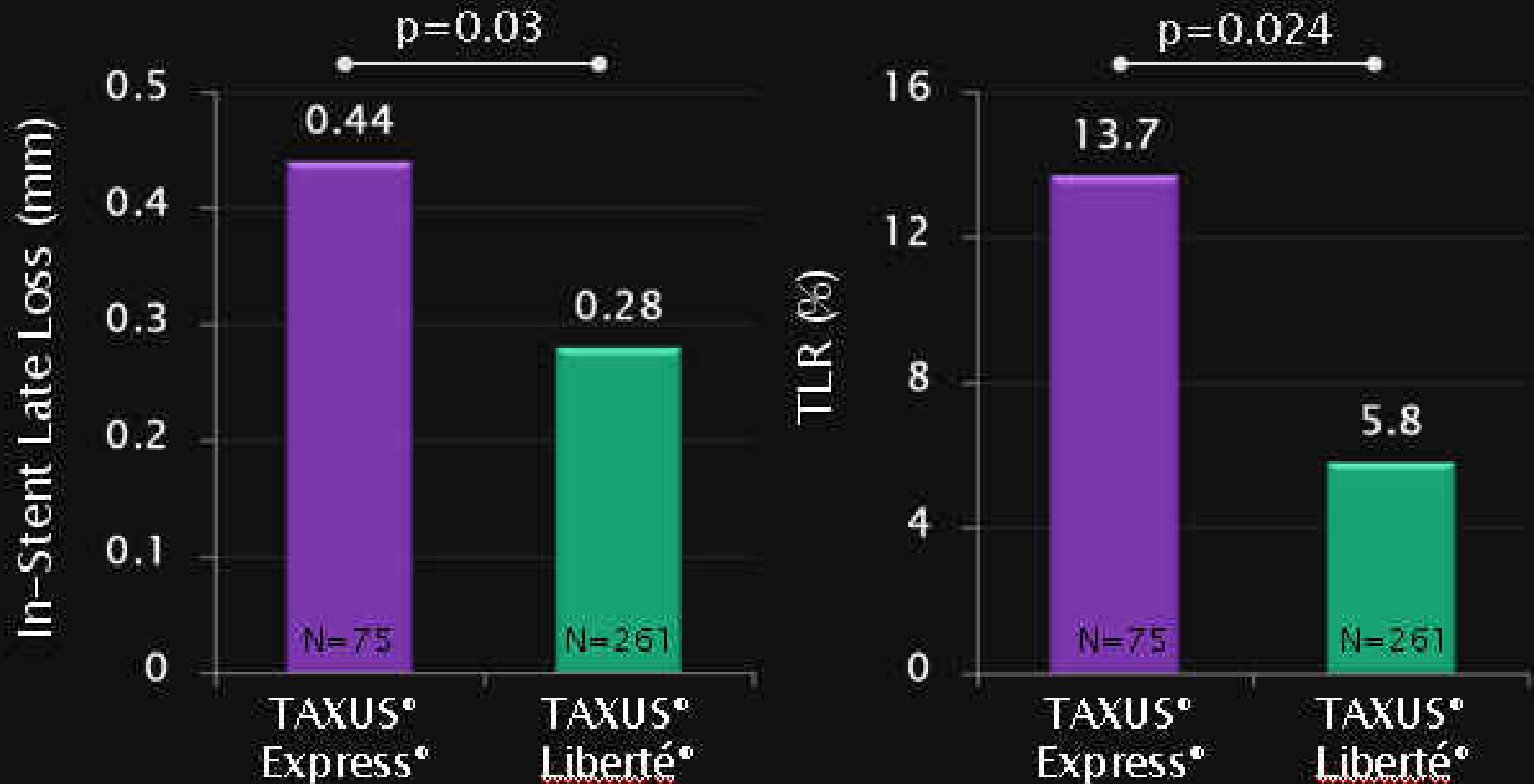
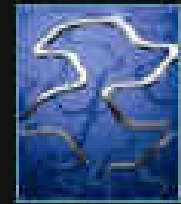
Reduced Risk of Restenosis in Small Vessels and Reduced Risk of Myocardial Infarction in Long Lesions With the New Thin-Strut TAXUS Liberté Stent

1-Year Results From the TAXUS ATLAS Program

Mark A. Turco, MD,* John A. Ormiston, MBChB,† Jeffrey J. Popma, MD,‡
Jack J. Hall, MD,§ Tift Mann, MD,|| Louis A. Cannon, MD,¶ Mark W. I. Webster,
MBChB,# Gregory J. Mishkel, MD,** Charles D. O'Shaughnessy, MD,††
Thomas F. McGarry, MD,‡‡ Lazar Mandinov, MD,§§ Keith D. Dawkins, MD,§§
Donald S. Baim, MD§§§

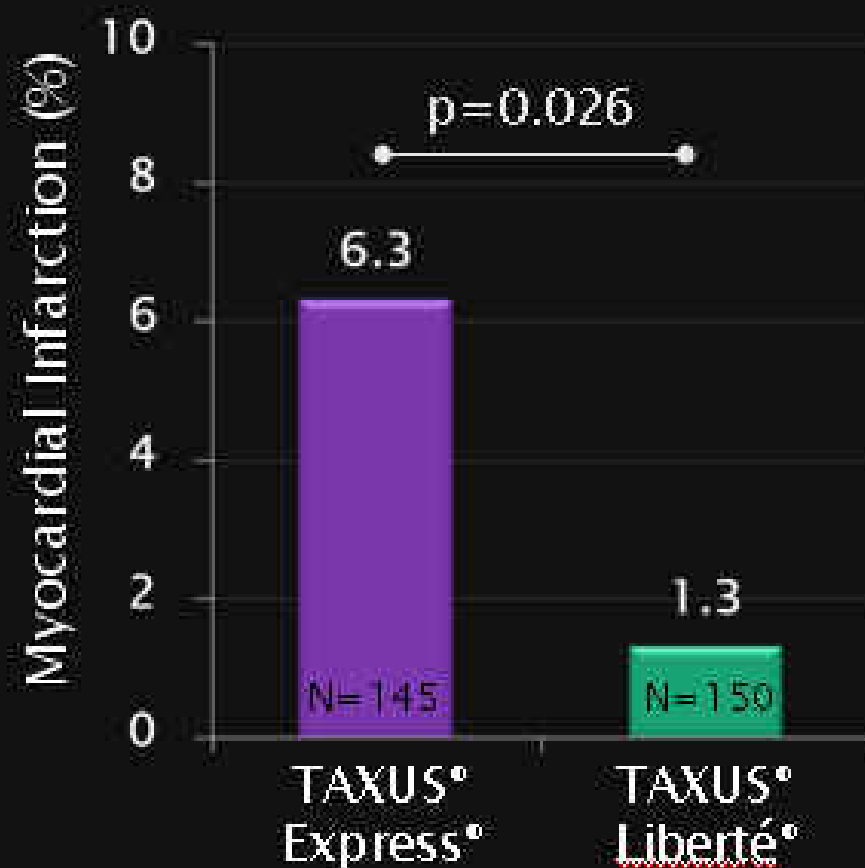
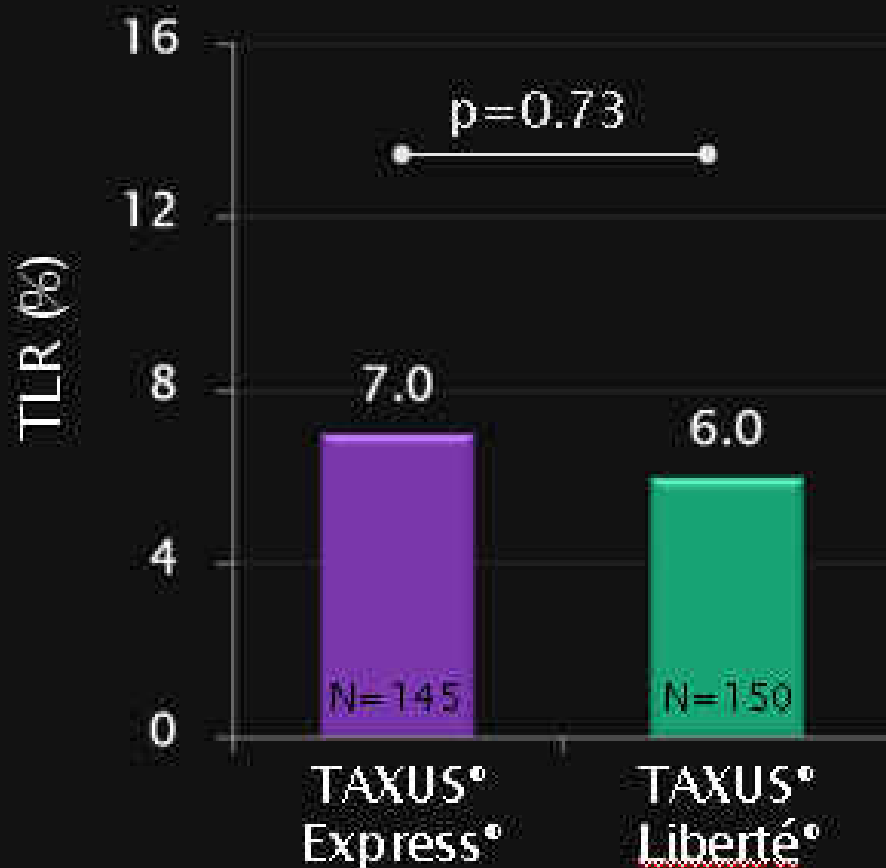
*Takoma Park, Maryland; Auckland, New Zealand; Boston and Natick, Massachusetts; Indianapolis,
Indiana; Raleigh, North Carolina; Petoskey, Michigan; Springfield, Illinois; Elyria, Ohio; and
Oklahoma City, Oklahoma*

TAXUS[®] ATLAS Small Vessel



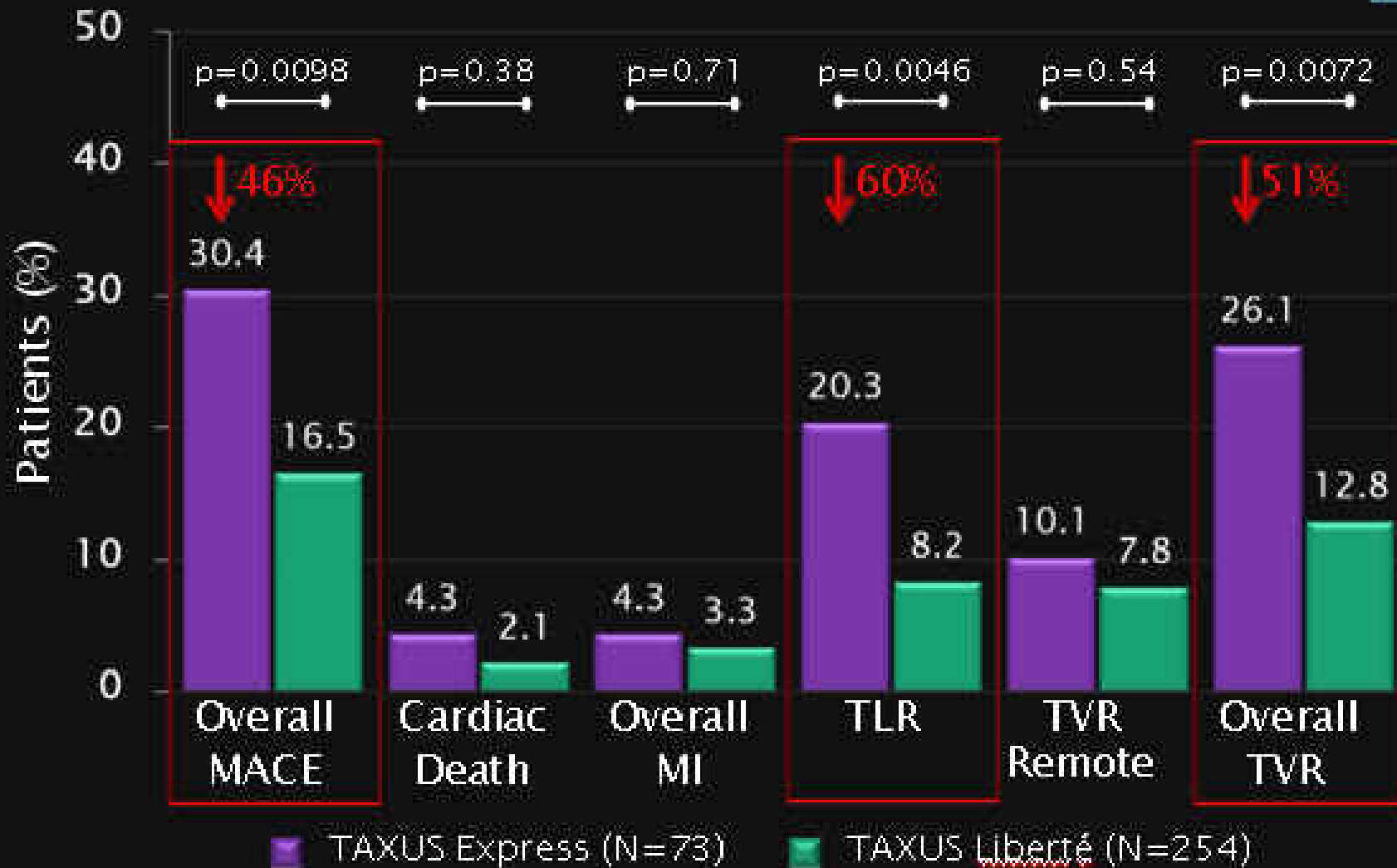
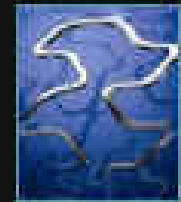
TAXUS[®] Liberté[®] angiographic superiority reflected in improved clinical outcomes in small vessel disease

TAXUS[®] ATLAS Long Lesion



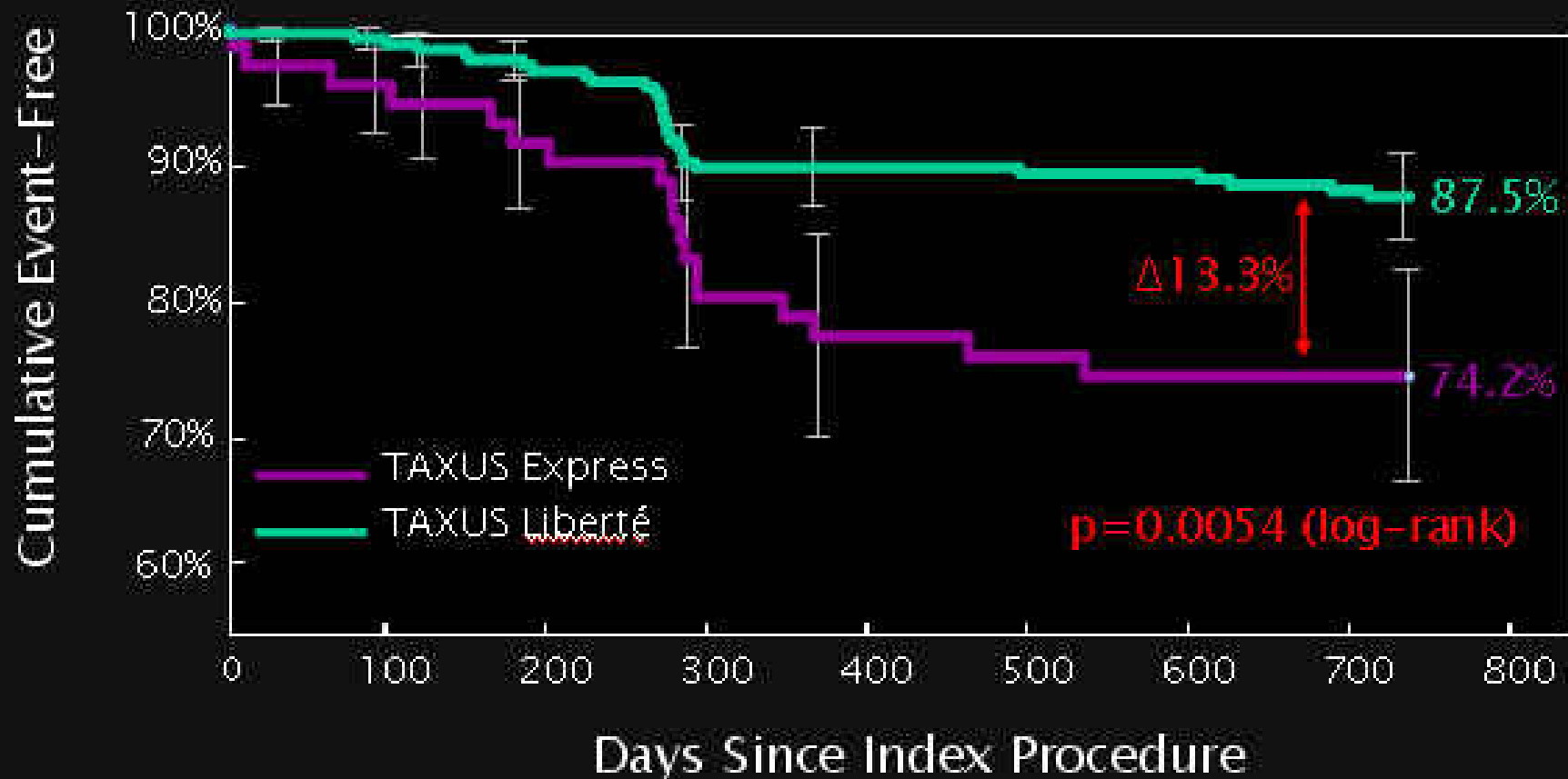
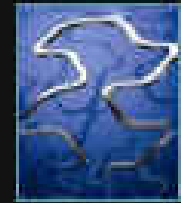
TAXUS[®] Liberté[®] has similar outcomes to TAXUS[®] Express[®], but lower rates of myocardial infarction when treating long lesions

ATLAS Small Vessel: 2-Year MACE rates



Binary Rates, Study Stent Population

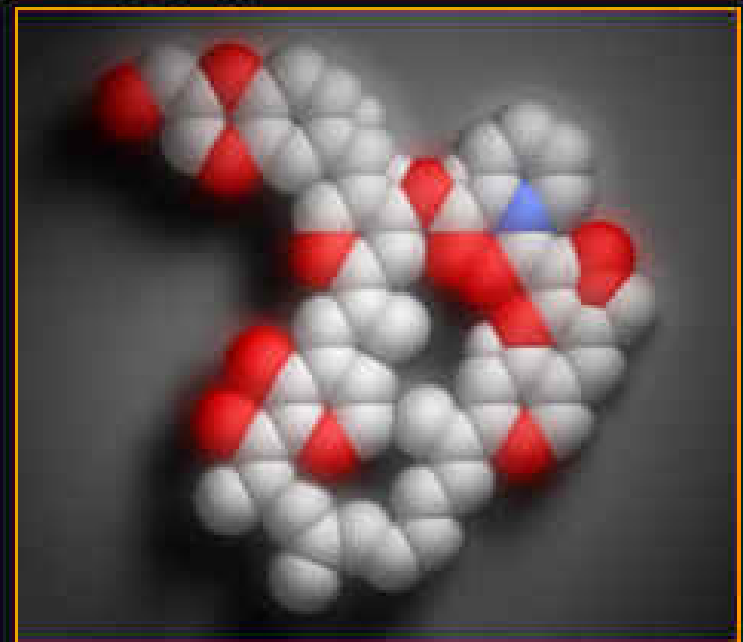
ATLAS Small Vessel: 2-Year TVR rates



Study Stent Population

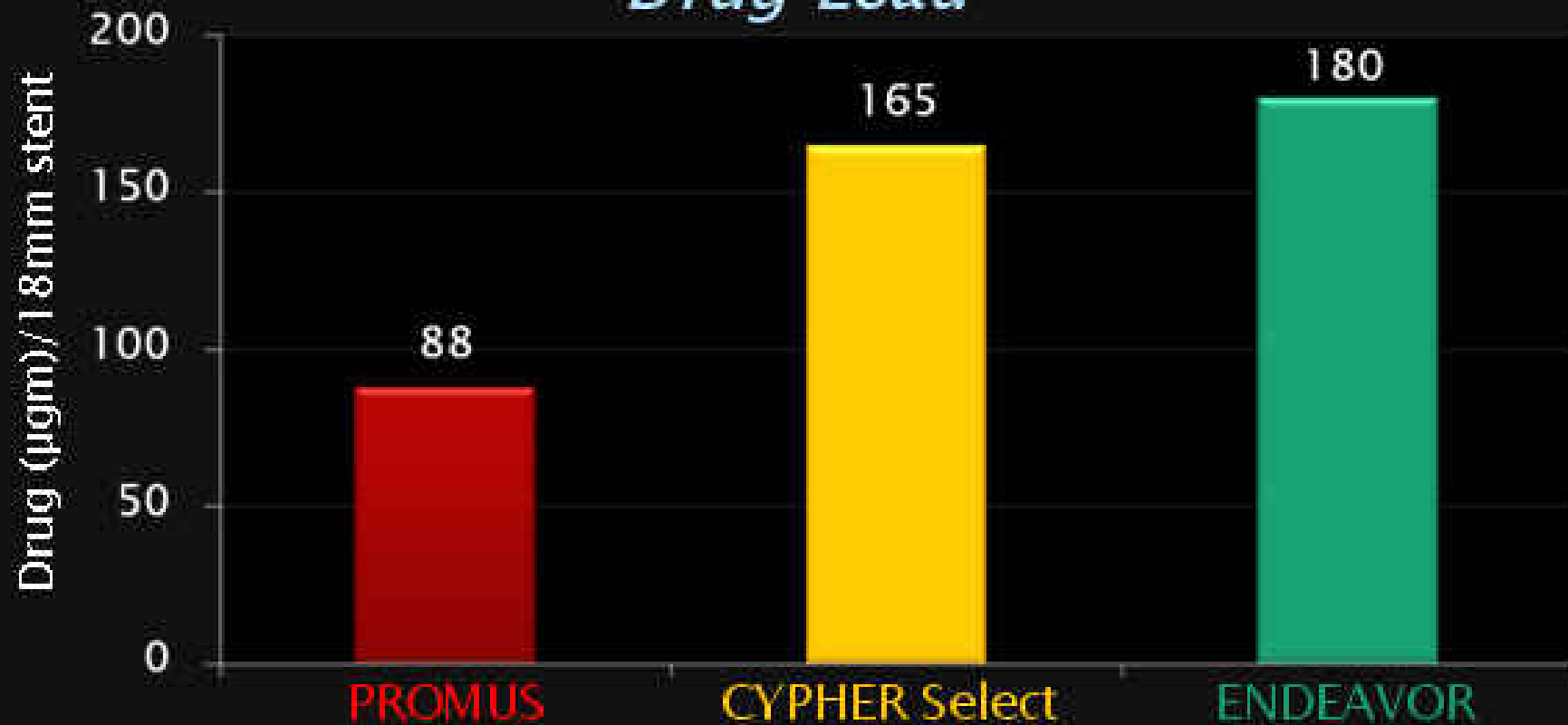
TAXUS Liberté Atom
Planned US Launch Q2 2009

PROMUS[®]
Everolimus
Eluting Coronary
Stent System







PROMUS™ Everolimus-Eluting Coronary Stent System

Drug Load



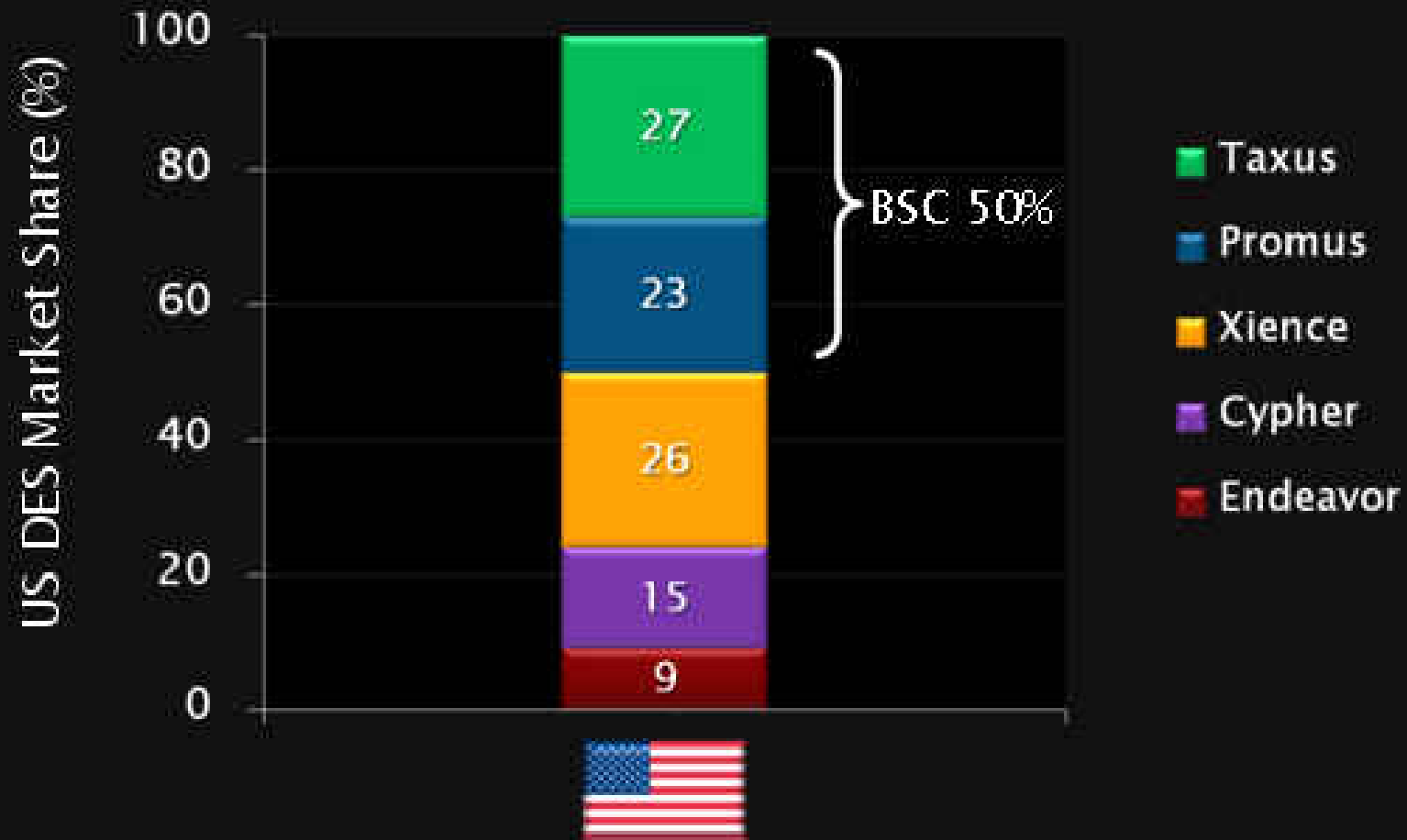
- 47% less drug than CYPHER
- 51% less drug than ENDEAVOR
- ~80% drug released within 28 days

Stent Platforms: Strut & Polymer Thickness*

	CYPHER	TAXUS Liberté	ENDEAVOR	PROMUS
Stent				
Strut Thickness	140µm	97µm	91µm	81µm
Polymer Thickness	14 x 2µm	14 x 2µm	6 x 2µm	7 x 2µm
Total	168µm	125µm	103µm	95µm

3.0 mm diameter stents, 500x magnification

Is the BSC Two Drug Strategy Working?

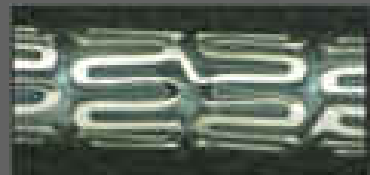


Source: MRG (March 2009)

BSC Two Drug Strategy: I

Paclitaxel

Element Stent

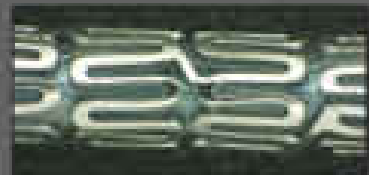


Trial
Complete
N=1488

TAXUS
PERSEUS

Everolimus

Element Stent

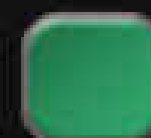
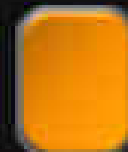
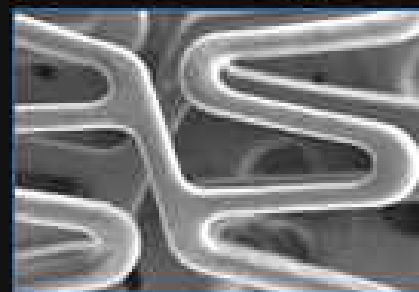
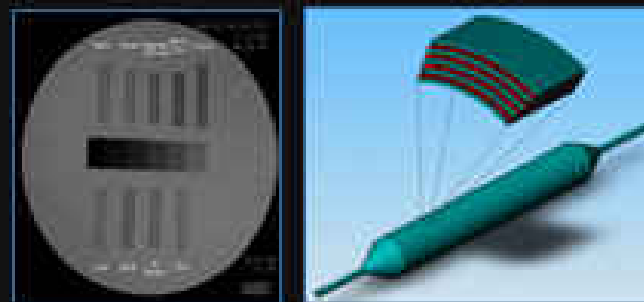
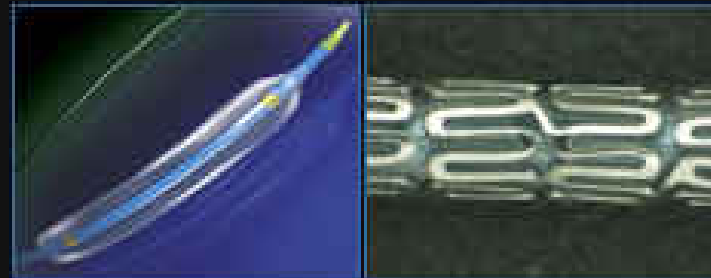


Trial
Started 1.09
N=1828

PROMUS
PLATINUM

Element Stent Platform

- Geometry designed for drug delivery
 - Four stent models
 - Consistent surface-to-artery ratios
- Apex™ balloon
 - Bi-component balloon
 - Multilayer
- Platinum Chromium Alloy
 - Radio-opaque
 - Thin Struts
 - High radial strength



Vision 0.0032"

Driver 0.0036"

Express 0.0052"

Liberté 0.0038"

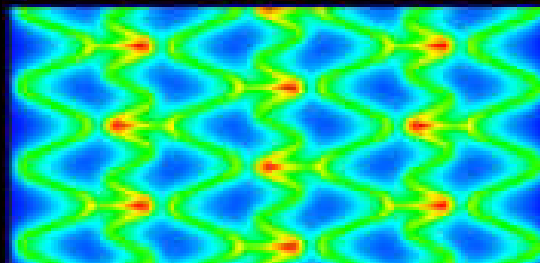
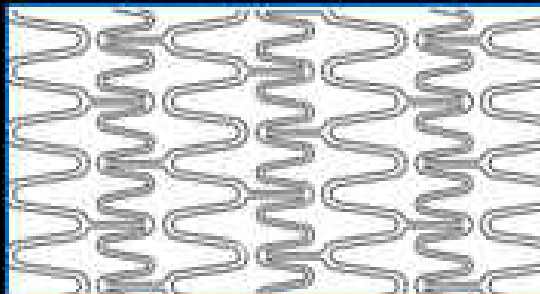
Element 0.0032"

TAXUS Stent Design

TAXUS Express²

Diam: 2.25 - 5.0mm

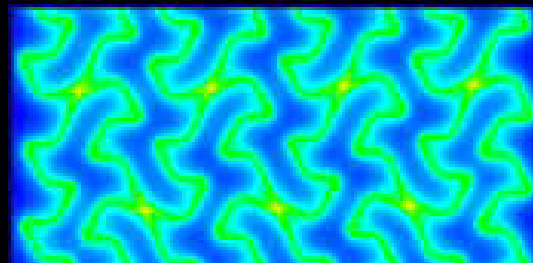
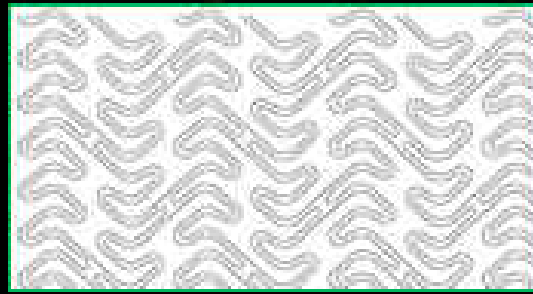
Stent Designs: 2
(WH + LV)



TAXUS Liberté

Diam: 2.25 - 5.0mm

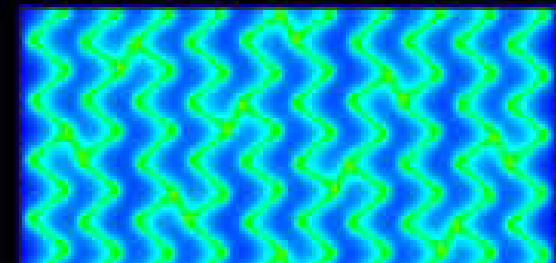
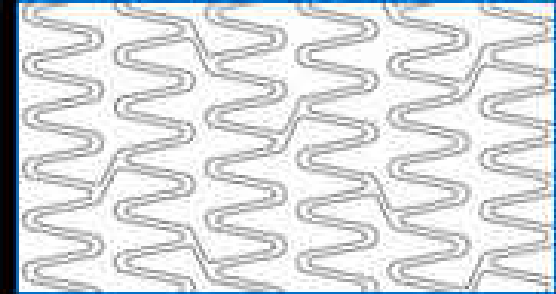
Stent Designs: 3
(SV + WH + LV)



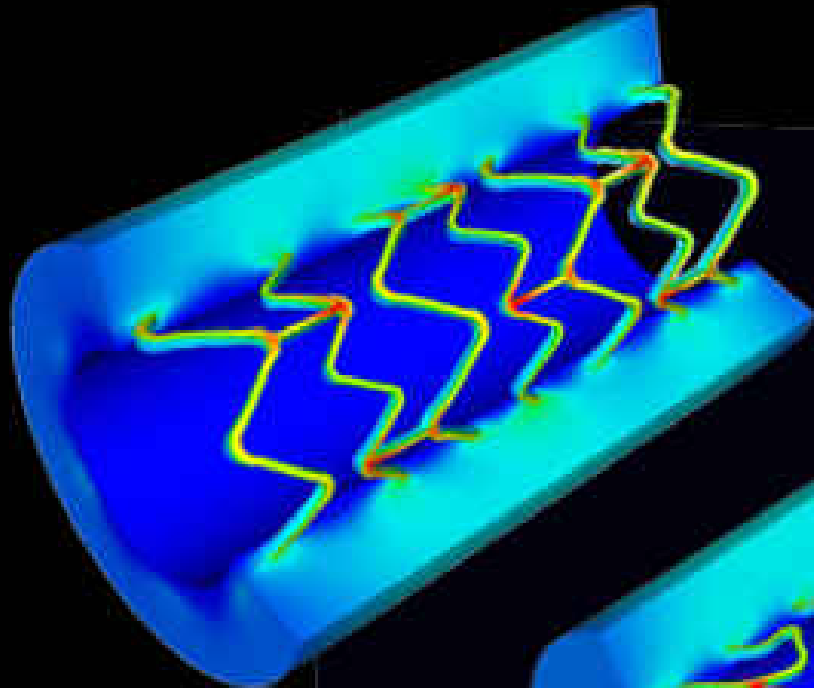
TAXUS Element

Diam: 2.25 - 5.0mm

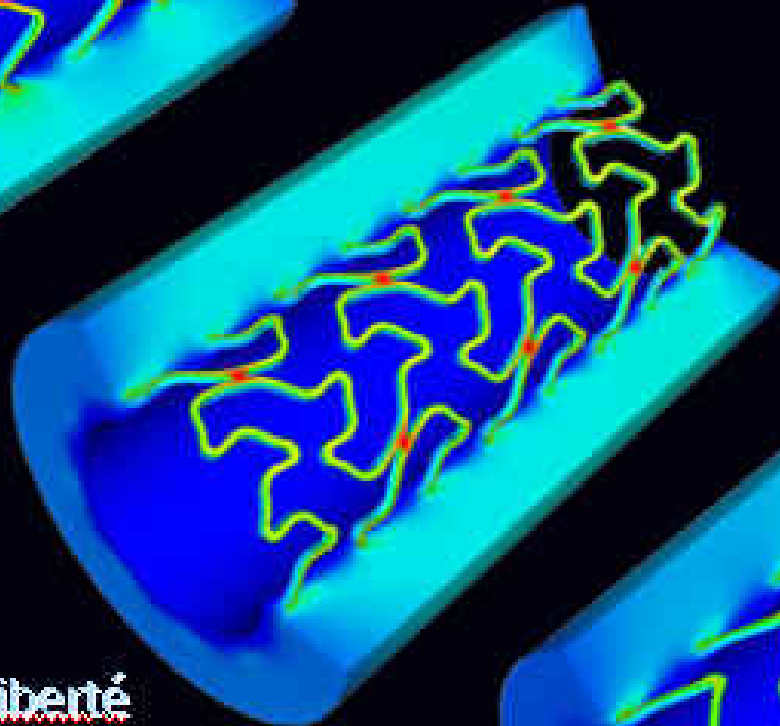
Stent Designs: 4
(SV + SWH + WH + LV)



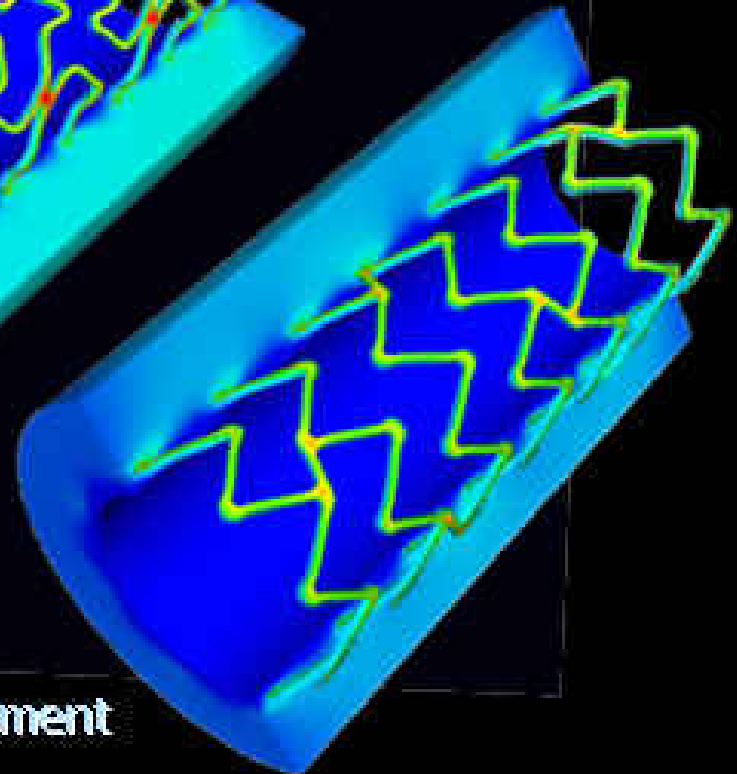
Allows for more consistent performance across diameter range



Taxus Express²



Taxus Liberté

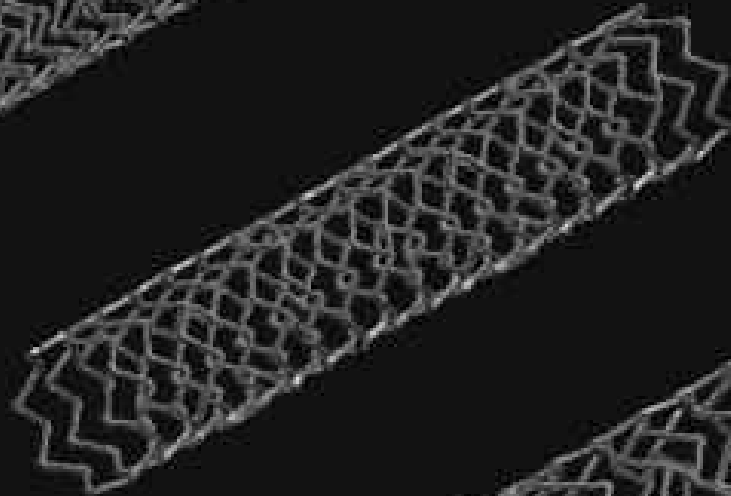


Taxus Element

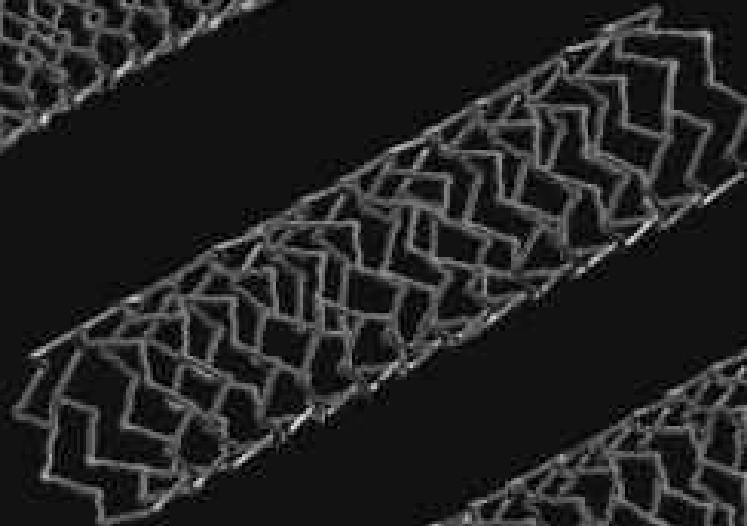
Element SV
(2.25)



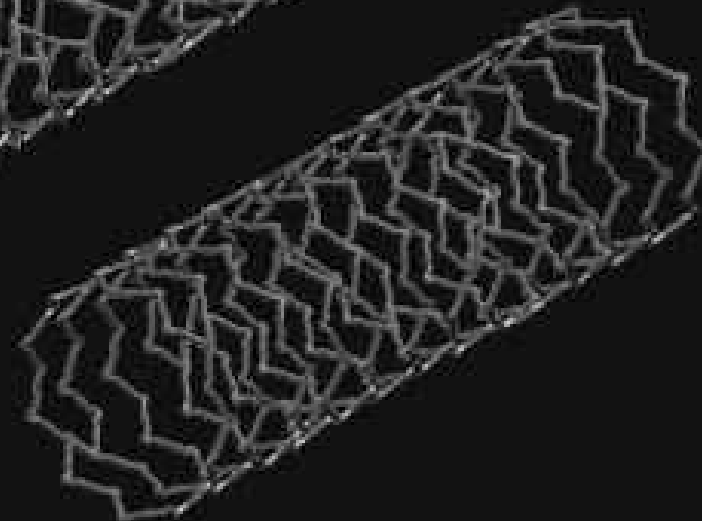
Element SWH
(2.50,2.75)



Element WH
(3.00,3.50)



Element LV
(4.00,4.50)



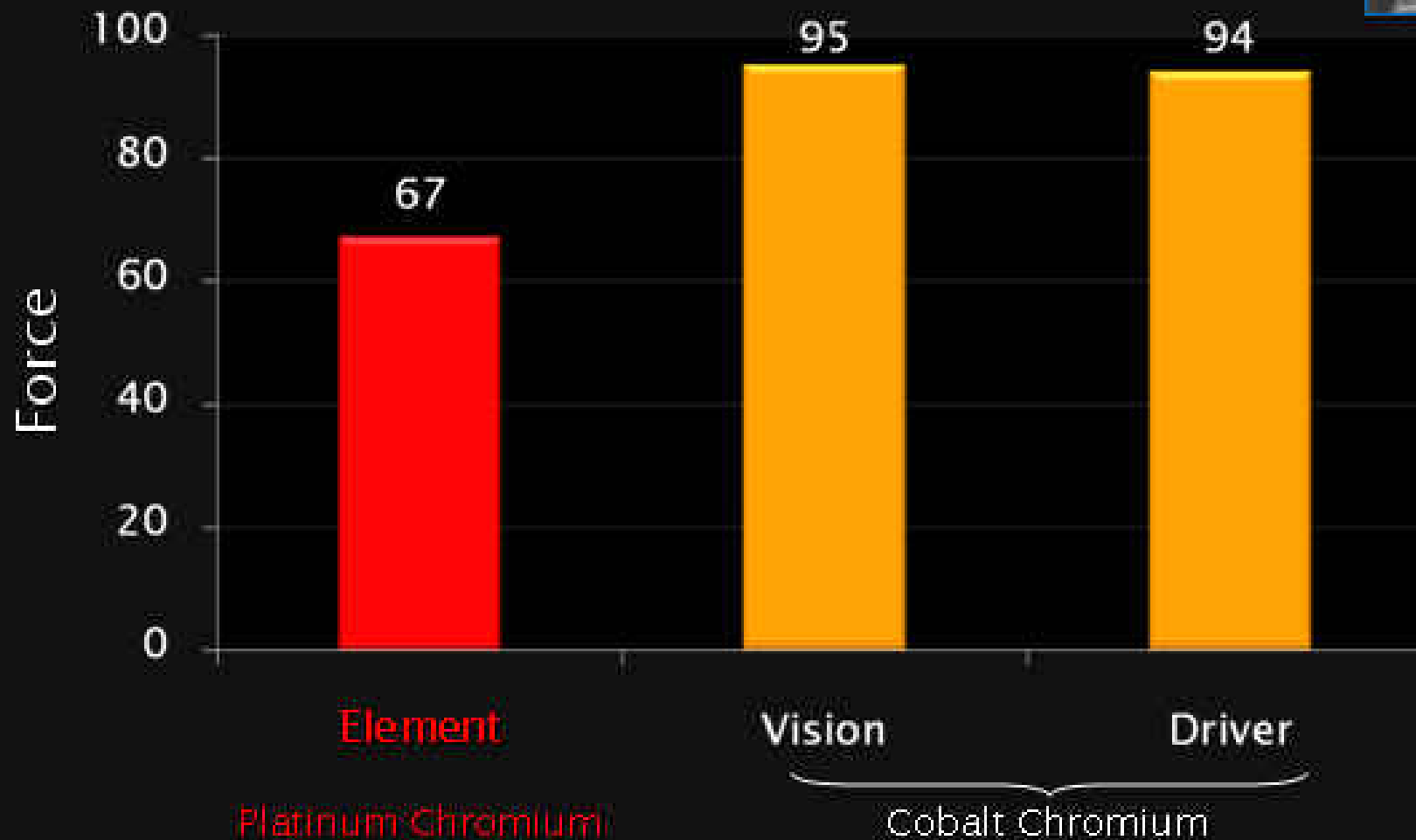
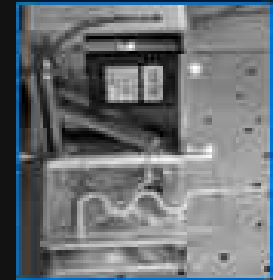
Element Stent
Designs

Element Stent Design: Platinum Chromium Alloy

	Elemental Composition by Weight (%)				Contribution to Stent Performance			
	316L Stainless Steel	Platinum Chromium Alloy	L605 (Cobalt Chromium Alloy)	MP35N (Cobalt Chromium Alloy)	Strength	Corrosion Resistance	Radio-opacity	MR Compatible
Iron	64	37	3.0 max	1.0 max				
Platinum	-	33	-	-	✓	✓	✓	✓
Cobalt	-	-	52	34		✓		
Chromium	18	18	20	20	✓	✓		✓
Nickel	14	9	10	35	✓			
Tungsten	-	-	15	-	✓		✓	✓
Molybdenum	2.6	2.6	-	9.75	✓	✓	✓	✓
Manganese	2.0 max	0.05 max	1.5	0.15 max				
Titanium	-	-	-	1.0 max				✓

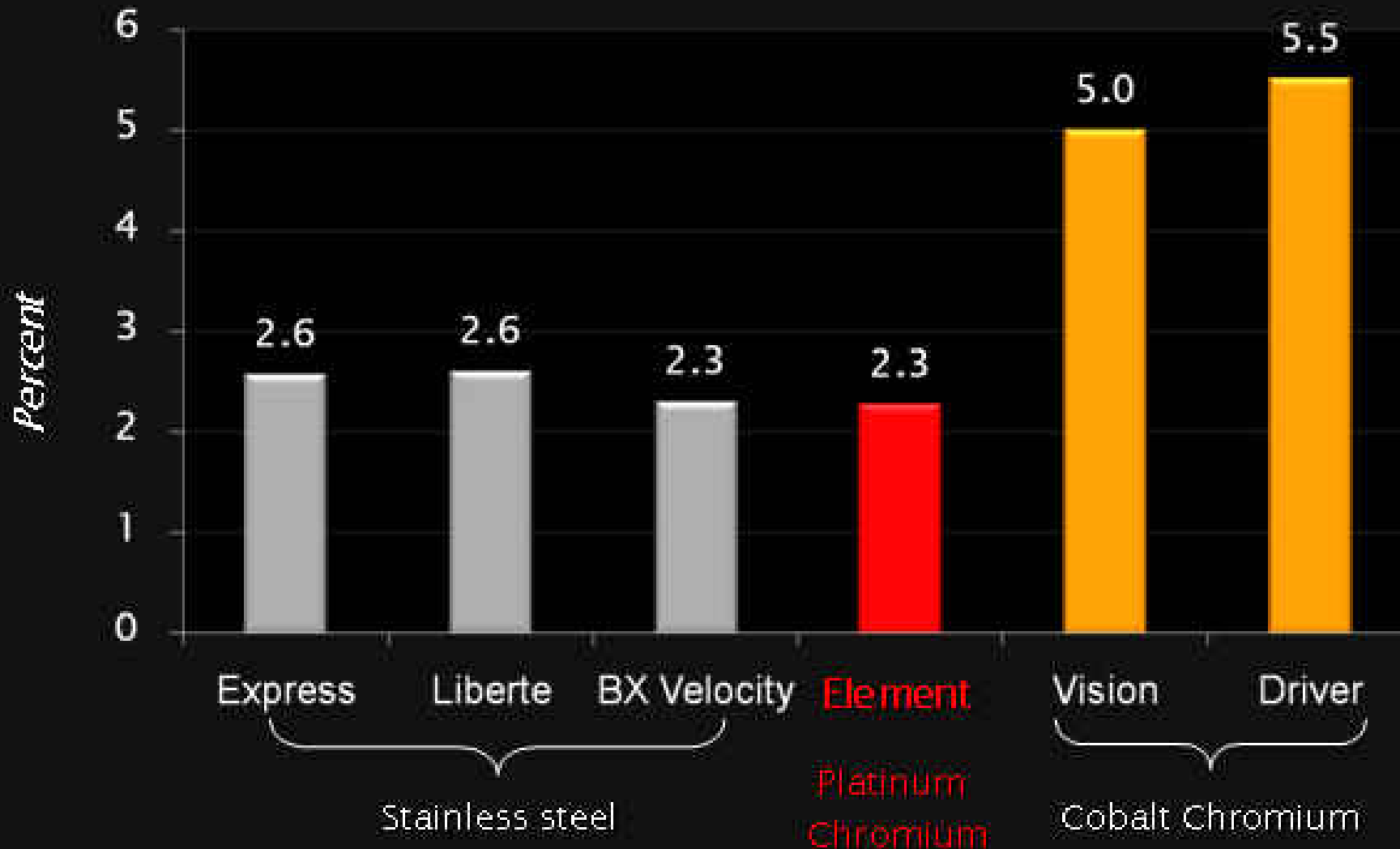
Platinum Chromium Alloy of the Element Stent Provides Enhanced Performance Benefits

Comparative Trackability**



**Trackability: Measures the ability of the stent delivery system to maneuver through a tortuous artery model. Lower forces indicate increased trackability and greater distal segment flexibility.

Comparative Recoil*



*Recoil: The percentage that the stent diameter decreases after balloon deflation. Lower recoil maintains better vessel lumen diameter after the balloon is deflated and withdrawn.

Next
Generation
DES



Next Generation DES Attributes

- **Safety**

- No Stent Thrombosis ('BMS' like)
- Shortened/No DAPT Requirement

- **Efficacy**

- Low Late Loss, Binary Restenosis
- Low TLR, Low Clinical Symptom Recurrence

Defining 'Healing' for NG DES

Differentiating NG Stent Designs

Stent Coating

Conformal vs Abluminal
Labcoat vs Rollcoat

Polymer

PLGA vs PLA
Polymer Load
Degradation Rate

Drug

PTX vs EVL
Dose, Release Kinetics

Defining 'Healing' for NG DES

Differentiating NG Stent Designs

Stent Coating

Conformal vs Abluminal
Labcoat vs Rollcoat

Polymer

PLGA vs PLA
Polymer Load
Degradation Rate

Drug

PTX vs EVL
Dose, Release Kinetics



ECM

STRUCTURE

Quiescent SMCs

Confluent EC Monolayer

Intact Basement Membrane

Minimal Chronic Inflammation



FUNCTION

Barrier Function

Non-Thrombogenic

Vasomotor Response

Lowering the Requirement for DAPT

heartwire



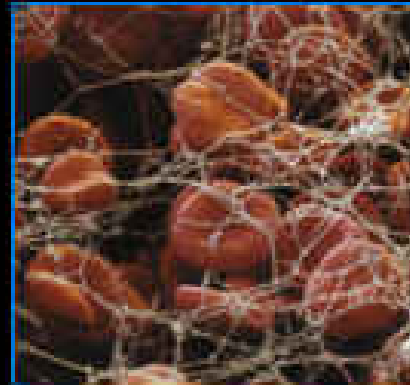
One in 10 stops taking clopidogrel because of "nuisance bleeding"

13 COMMENTS · DEC 24, 2008 09:15 EST

Washington, DC - New observational data highlight the problem of "nuisance bleeding" on **clopidogrel** (Plavix, Bristol-Myers Squibb/Sanofi-Aventis) therapy following stent implantation, with as many as 85% of patients experiencing easy bruising, bleeding from small cuts, and minor hemorrhages from broken capillary vessels [1].

"We typically report the more internal or alarming bleeding, but nuisance bleeding is not reported intensively so far, and people try to ignore it, but from the patient perspective this is really important," said senior investigator **Dr Ron Waksman** (Washington Hospital Center, DC). "It really is a nuisance. They live with it on a daily basis, and they don't like it. Even if they adhere to antiplatelet therapy, there is a price to pay for that." [Read full article »](#)

(Roy P et al. *Am J Cardiol* 2008; 102: 1614-1617.)



BSC LABCOAT ACQUISITION



UPDATE 1-Boston Scientific buys stent polymer maker

Thu Jan 8, 2009 3:02pm GMT

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MARKET NEWS

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- [STOCKS NEWS US-Earnings diary for Jan 9](#)
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- [More Business & Investing News...](#)

* Irish company makes polymer for Boston Scientific stents

* Terms of the acquisition not disclosed

* European approval for technology to be sought this year

CHICAGO, Jan 6 (Reuters) - Boston Scientific Corp ([BSX.N](#)) on Tuesday said it acquired a privately held Irish company

that has developed a biodegradable polymer for use with its drug-eluting stents that prop open clogged heart arteries.

The company, Labcoat Ltd of Galway, Ireland, has completed a clinical trial of its polymer containing the drug paclitaxel on Boston Scientific's bare-metal Liberté stent. The data will be used to support an application for European regulatory approval that is expected to be submitted in the first half of this year.

Polymers bind drugs to stents that help prevent relogging of the vessel after the tiny metal-mesh devices are inserted.

Terms of the deal were not disclosed.

Labcoat's biodegradable technology is designed to improve healing of the vessel wall by reducing the amount of polymer and drug to which it is exposed.



Second Generation Coating Technology



Conformal Coating

- Polymer-drug coated on to 360° of stent strut
- Polymer coating on entire surface area of stent (circumferential)
- Excess polymer and/or drug?



Bioerodable, abluminal coating

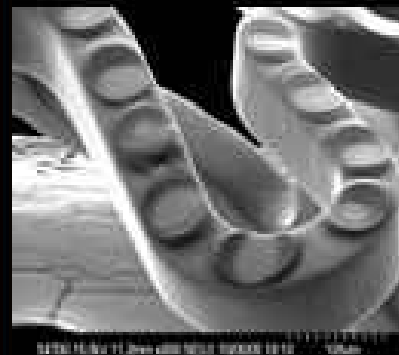
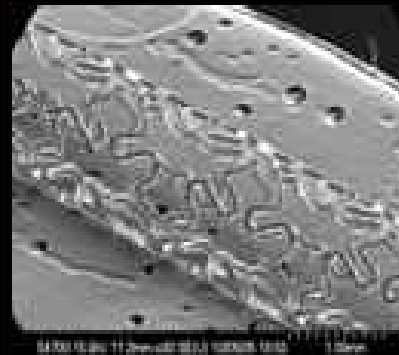
- Droplets of polymer-drug coating on the outside surface of the stent only
- Reduced amount of drug and polymer
- BMS surface on three sides
- Drug only where required



Abluminal Coating JA™ Coating Technology



- Proprietary Abluminal Bioerodable Micro Drop Structure
 - Minimal Polymer
 - Controlled Drug Release
 - Adjustable Kinetics Possible
 - No strut to strut or balloon to strut polymer interaction
- Coating applied to any stent design either bare or pre-mounted



JACTAX HD Trial

PI: Eberhard Grube

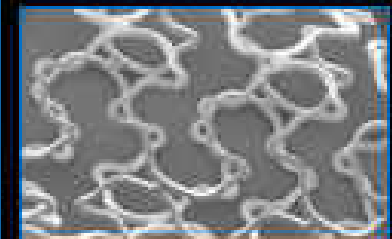


Stent Platform

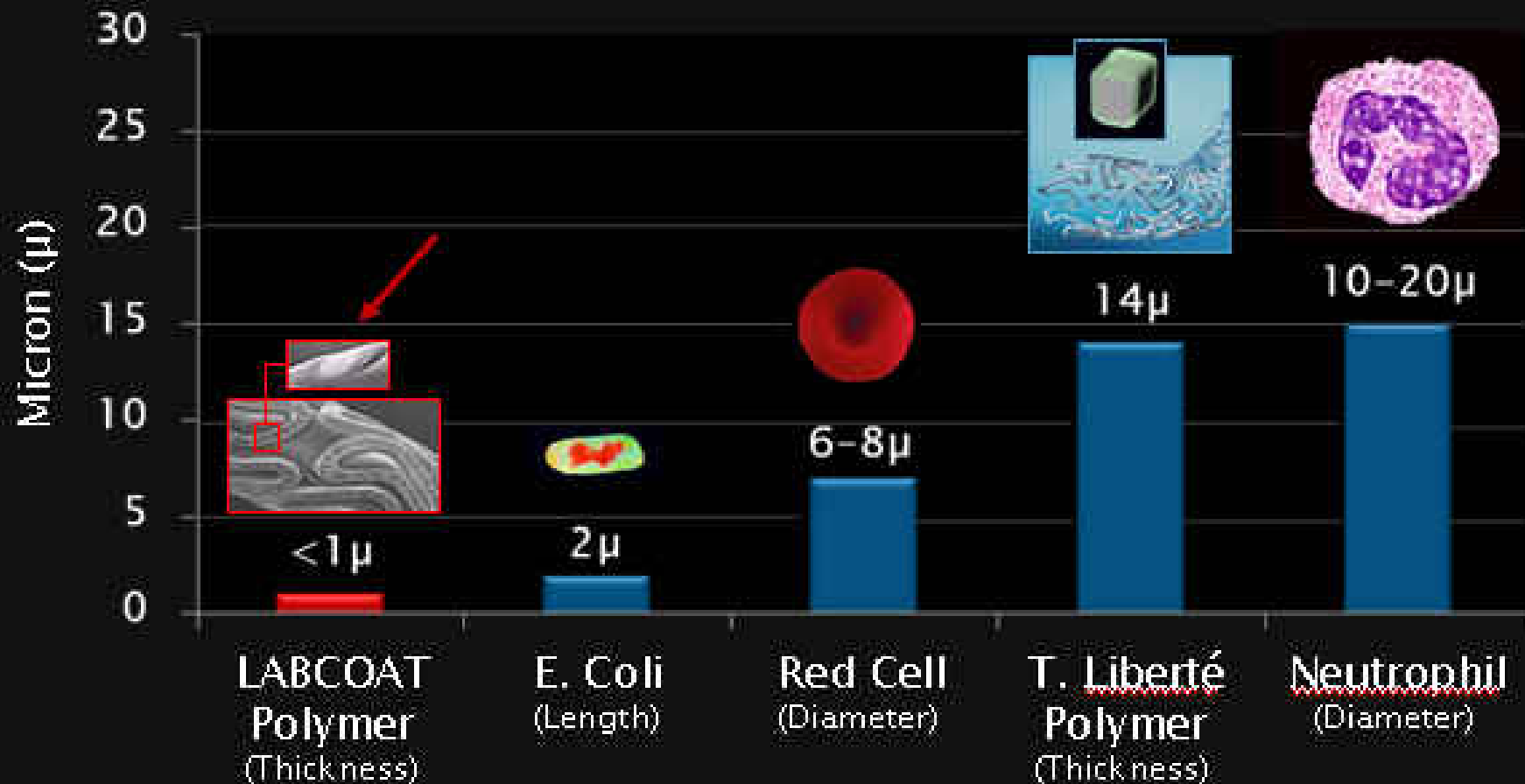
- Liberté[®] Pre-mounted stent (BSC)

JA[®] Coating

- 9.2 μg . of Paclitaxel and 9.2 μg . DLPLA (16 mm)
- 2700 microdots (16 mm)
- Mass of polymer approx 3.4 ng. per microdot
- < 1 micron thick, abluminal and low molecular weight biodegradable polymer decreases persistence time

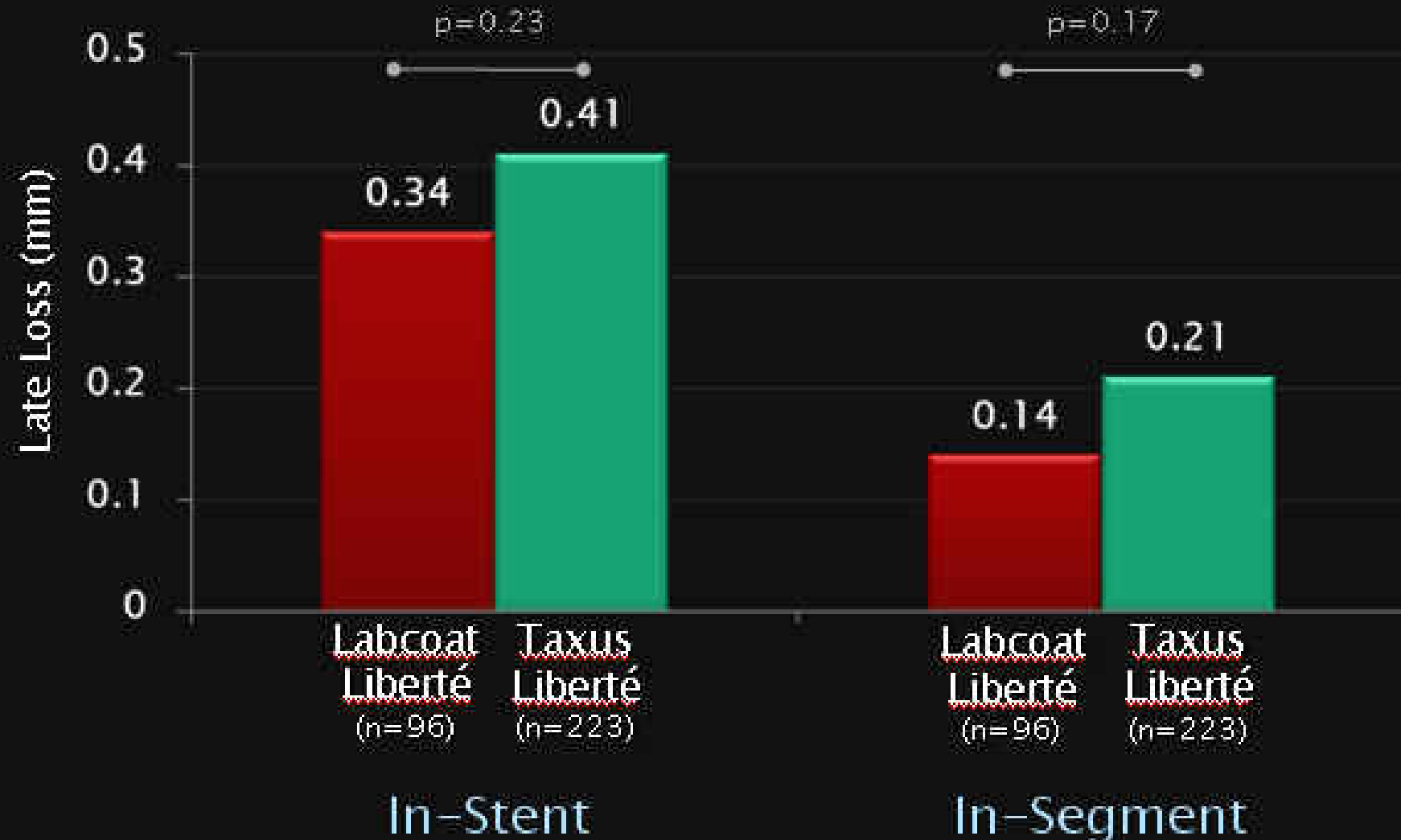
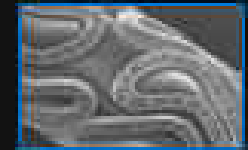


Labcoat Relative Polymer Thickness

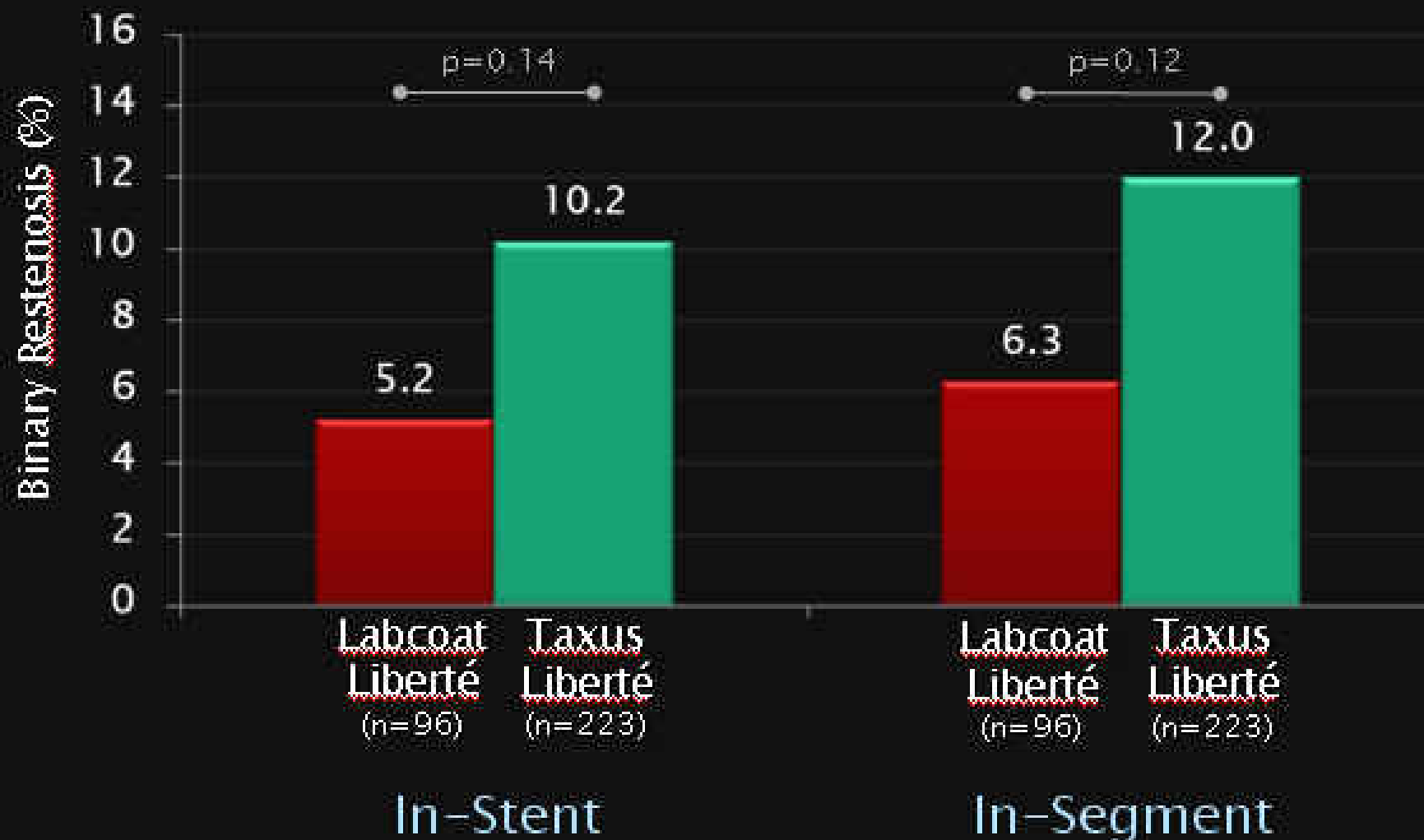
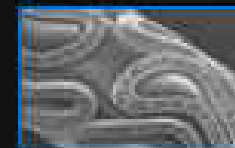


LABCOAT = Minimal Drug + Ultrathin Bioerodable Abluminal Polymer

JACTAX HD Results vs. ATLAS Matched (9 months)



JACTAX HD Results vs. ATLAS Matched (9 months)



BSC Two Drug Strategy: II

Paclitaxel

Everolimus

Next Generation DES

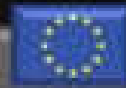
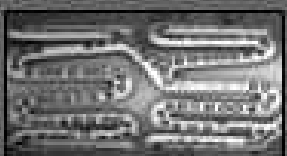
Low Drug Dose, Abluminal Delivery, Bioerodable Polymer → Short DAPT

Labcoat Liberté

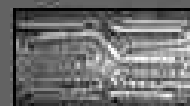


Trial Complete
N=103

Labcoat Element



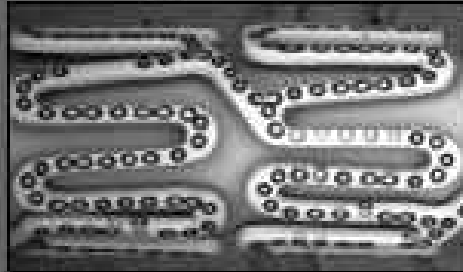
JacPro



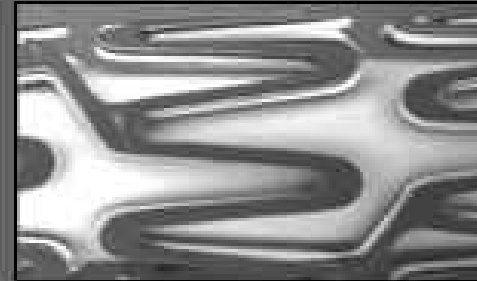
Evolution



JacPro



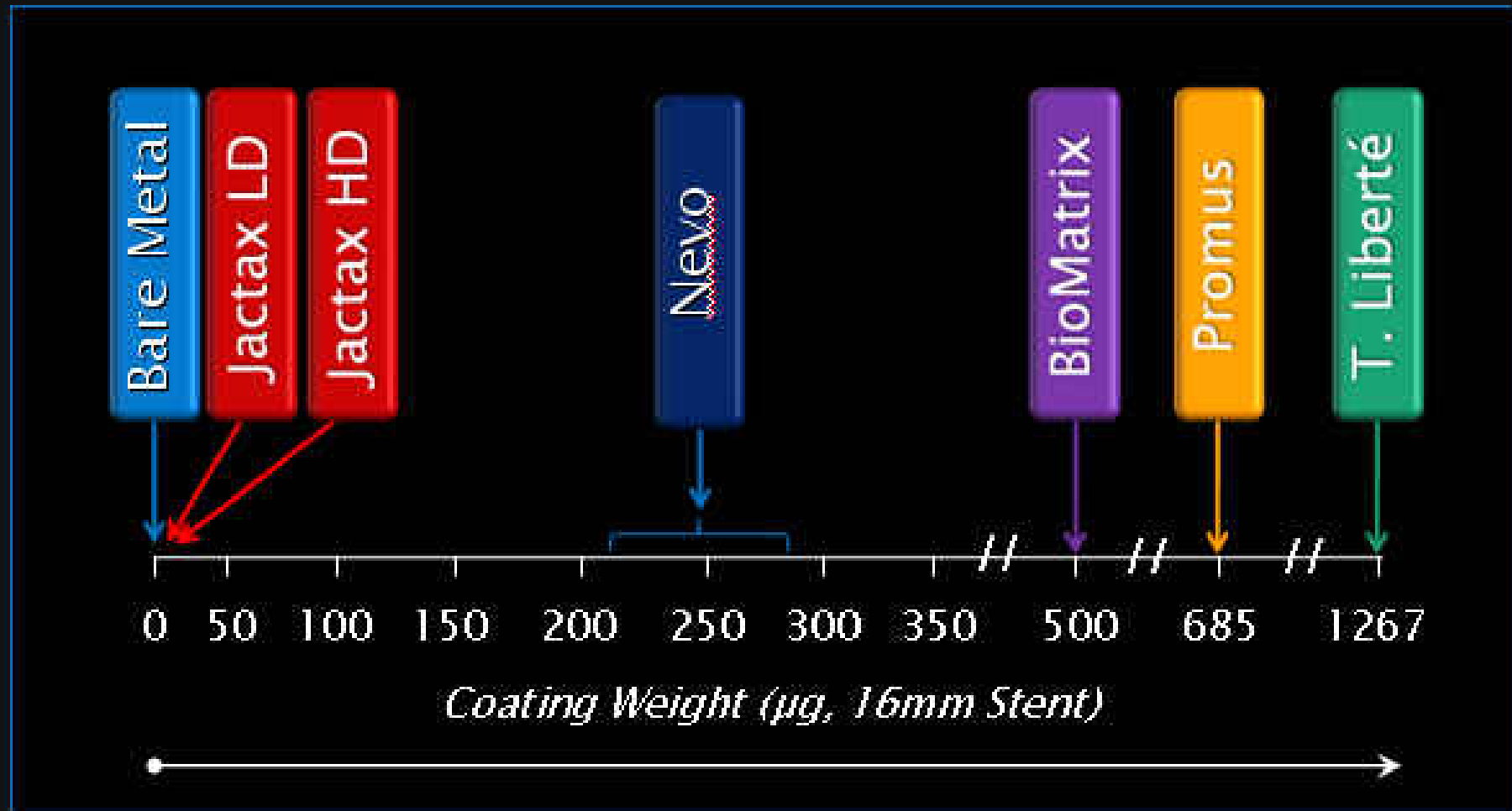
Evolution



Labcoat Element	TAXUS Element	Stent (16mm Workhorse)	Evolution	Promus Element
PLA	-	Biodeg Polymer	PLGA	-
10 - 18	970	Coat Wt (μg)	100 - 200	604
5 - 9	85	Total Dose (μg)	45 - 90	84
2 - 4mo	>12mo	Drug Gone (months)	2 - 3mo	3 - 4mo

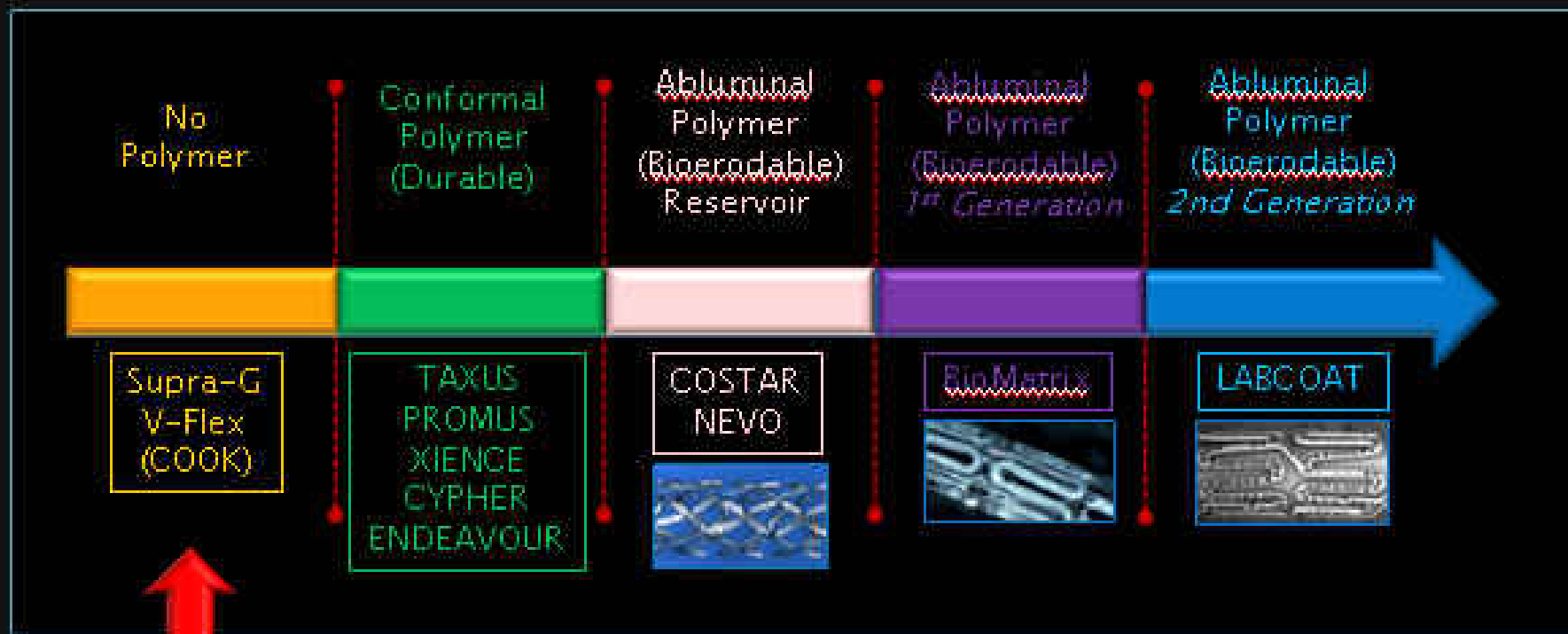
Next Generation DES aiming for 'BMS' like function within 4 months

Relative Drug Coating Weights



Evolution of Stent Based Drug Delivery

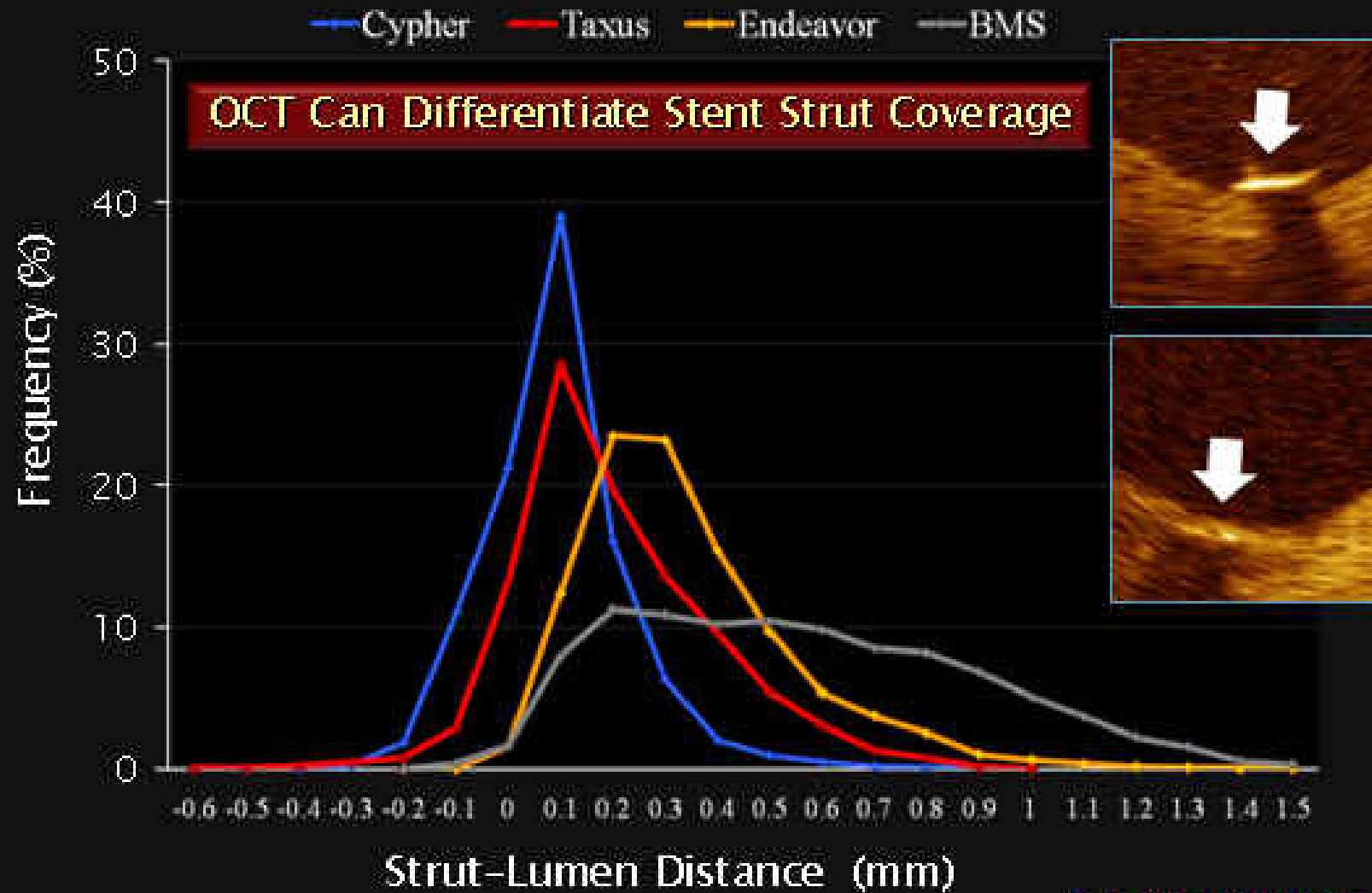
LABCOAT = Minimal Drug + Ultrathin Bioerodable Abluminal Polymer



Is 'No Polymer' Drug Delivery a Viable Option?

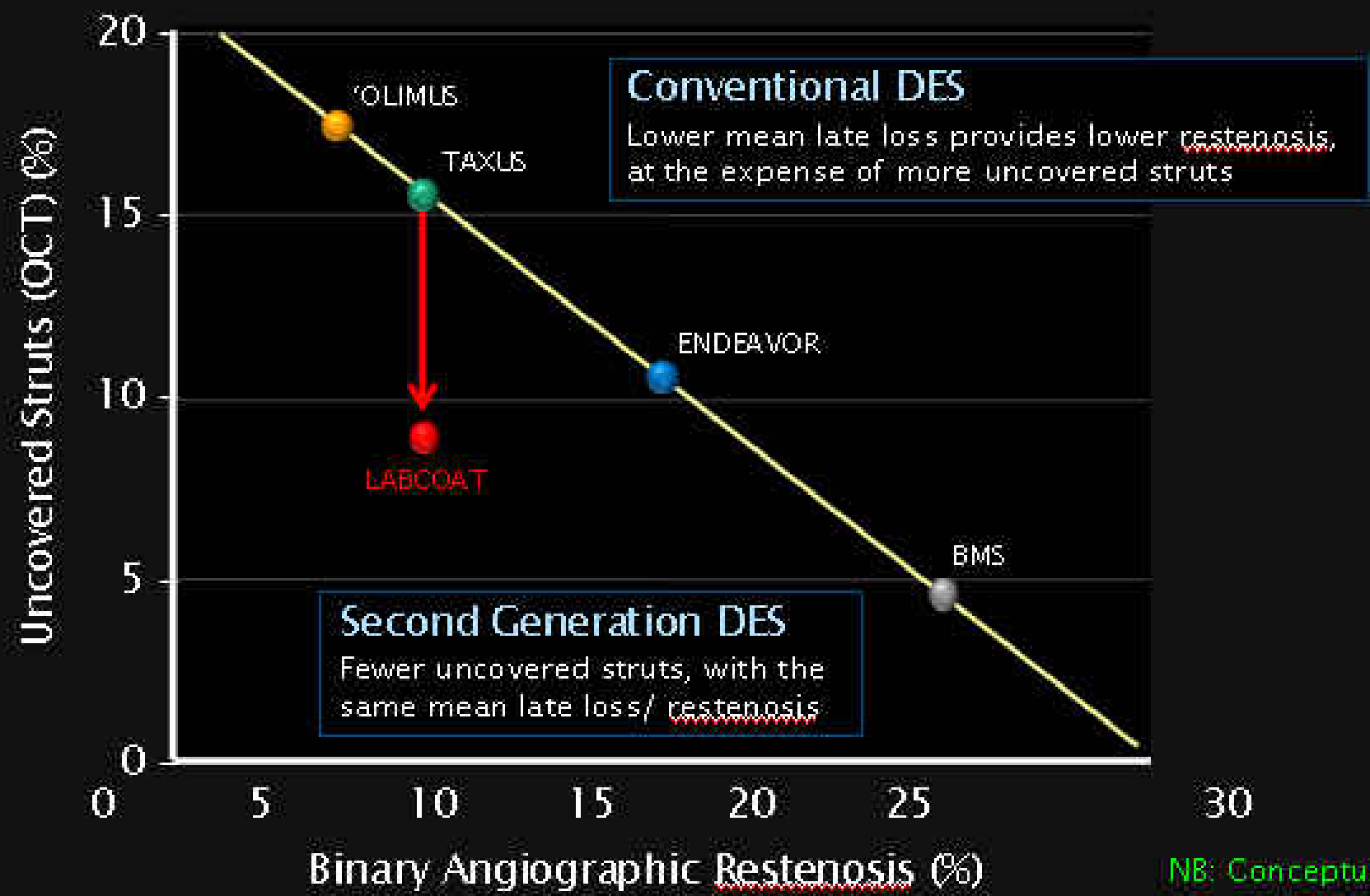
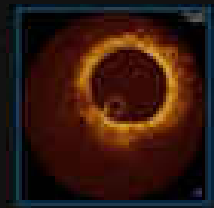
ODESSA Trial: Strut Level Analysis (6 months)

Frequency Distribution of Strut-Lumen Distance (53,047 struts)



The *Real* Second Generation DES Concept ?

Same angiographic restenosis with better strut coverage



Conclusions:

- The BSC position is robust and the pipeline healthy
- The TAXUS program provides an unparalleled dataset attesting to safety and efficacy
- Unique Two Drug/Platform position resulting in leading market share
- Next Generation Dual Drug ELEMENT platform under clinical evaluation with planned European launch Q4 2009
- Labcoat, ultrathin abluminal bioerodable polymer + minimal drug, another unique offering...