Advancing Outcomes with Next Generation DES

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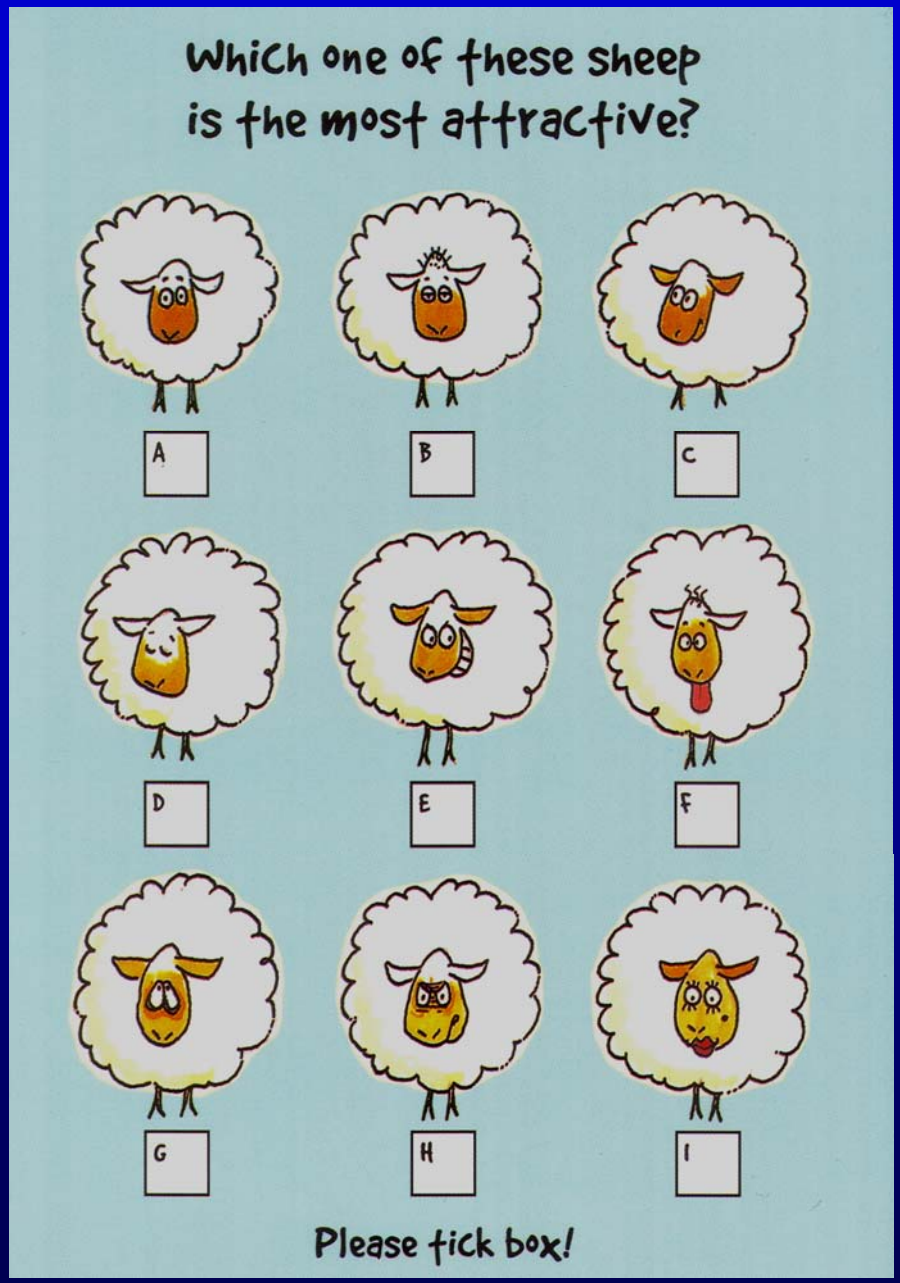
Potential Conflicts of Interest

- **Strategic and Scientific Advisory Boards:**
  Medtronic Vascular, Boston Scientific


Which one of these sheep is the most attractive?
A
B
C
D
E
F
G
H
I
Please tick box!

The Ideal DES

- Remarkable ease of use
- Unparalleled efficacy
  - Suppression of neointimal hyperplasia
- Impeccable safety
  - No adverse effects on vessel function or flow dynamics
  - No risk of LST or VLST
  - No need for more than short term DAPT

Desirable Technical Qualities in a DES

- Easy to deliver, pushable and trackable
- Low profile but visible
- Flexible in a crimped state
- Flexible and conformable in an expanded state
- Complete or near-complete apposition
- Good scaffolding and excellent radial strength
- Minimal vessel and intimal injury
- Thromboresistant materials
- Rapid re-endothelialization
- Functional endothelial layer (NO producing)
- Reliable and consistent inhibition of NIH
- Minimal or no long term inflammation
- No persistent responses or long term safety concerns
- Available in the widest range of sizes and lengths
- Competitively priced and on consignment

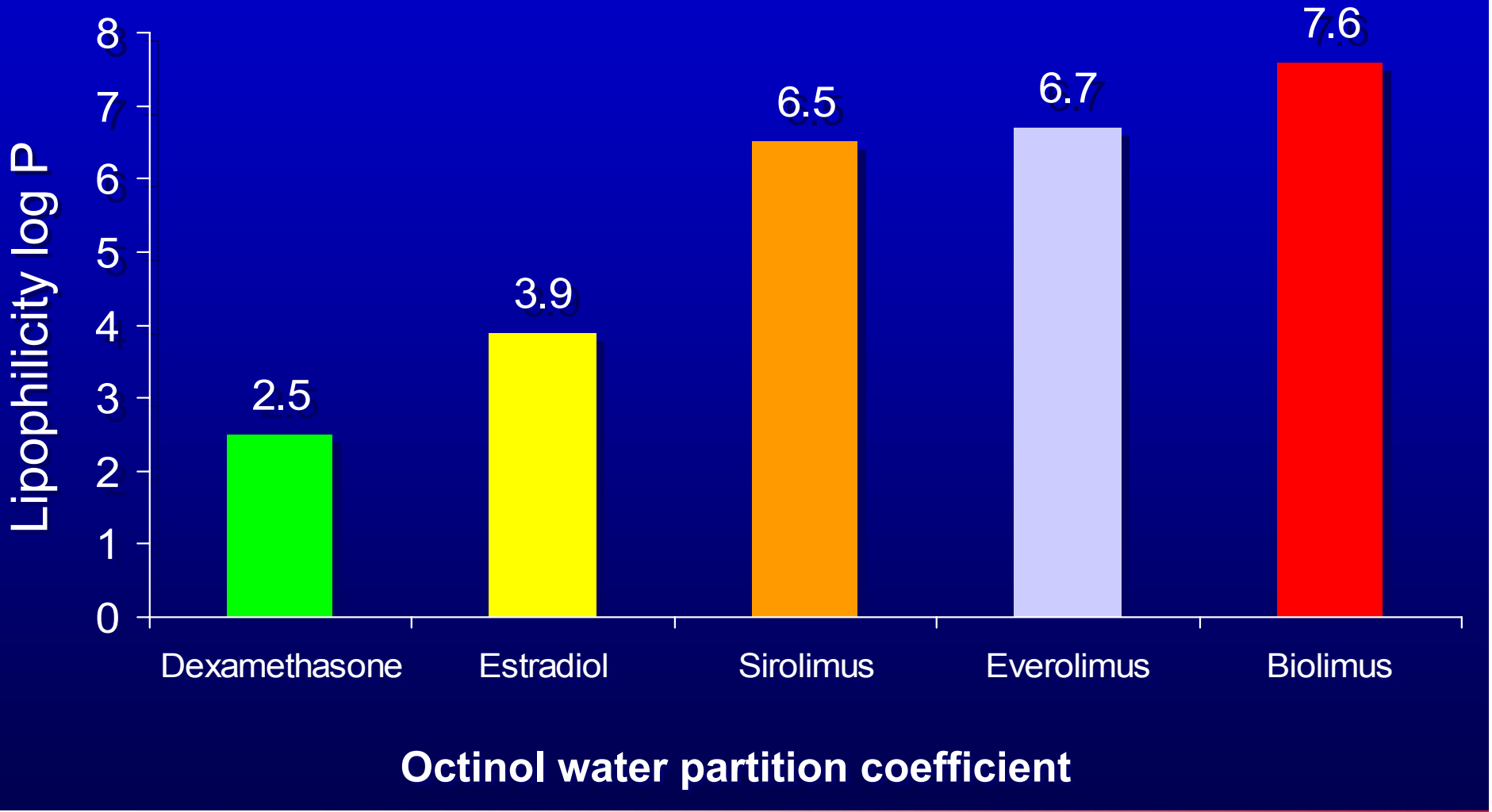
Drug Eluting Stent Landscape

- Abbott
  - Xience V
  - BVS
- Biosensors
  - BioMatrix
- Biotronik
  - Abs Magnesium
- Boston Scientific
  - Taxus Liberte
  - Promus
  - Taxus Element
  - Promus Element
- Cardiomind
  - Sparrow
- Cordis
  - Cypher
  - Nevo
- Elixir Medical
- Medtronic
  - Endeavor
  - Resolute
- Terumo
  - Nobori

Drugs

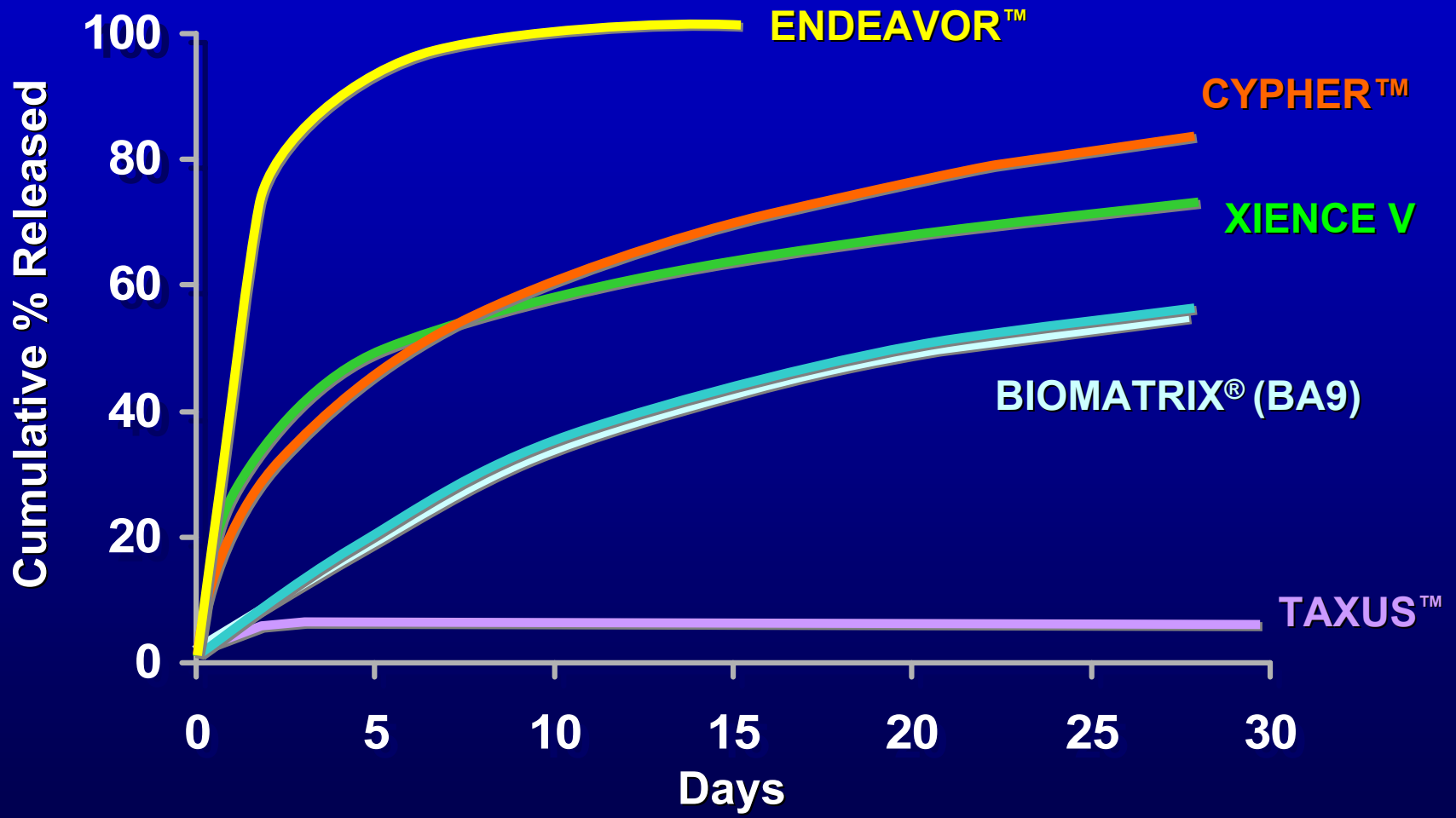
Stent	Drug	Mol.mass	Formula
Cypher Nevo	Sirolimus	914.17	$C_{51}H_{79}NO_{13}$
Xience V Promus Promus Element	Everolimus	958.224	$C_{53}H_{83}NO_{14}$
Exella	Novolimus	900	$C_{50}H_{77}NO_{13}$
BioMatrix Nobori	Biolimus A9	986.29	$C_{55}H_{87}NO_{14}$
Endeavor End Resolute	Zotarolimus	966.2	$C_{52}H_{79}N_5O_{12}$
Taxus Liberte Taxus Element	Paclitaxel	853.91	$C_{47}H_{51}NO_{14}$

Lipophilicity



Octinol water partition coefficient

Comparative Elution Profile



Generational Changes in Stent Specs

	Elemental Composition by Weight %			
	316L (Stainless Steel)	Platinum Chromium Alloy	L605 (Cobalt Chromium Alloy)	MP35N (Cobalt Chromium Alloy)
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

Stent Strut Thickness

Cypher™	Express®	Liberté®	Driver™	Vision™	Element™
0.0055" Stainless Steel	**0.0052"** Stainless Steel	**0.0038"** Stainless Steel	**0.0036"** MP35N	**0.0032"** L605	**0.0032"** Platinum Chromium

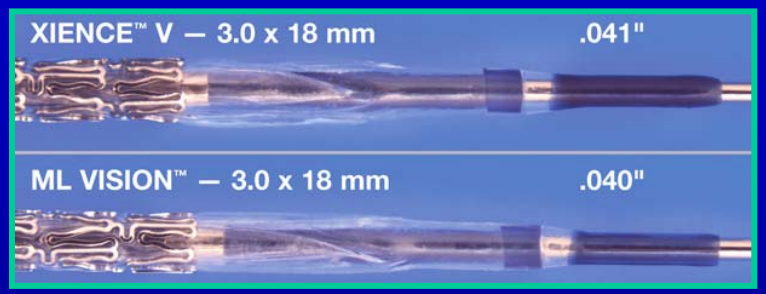
Thinner Stent Struts, Less Polymer Coating, Lower Drug Load

Stent	Strut Thickness	Polymer Thickness	Drug Load	Shape
Cypher	140 μm	12.6 μm	~10 ug/mm	Wedge
Taxus Express	132 μm	16 μm	1 ug/mm2	Wedge
Taxus Liberte	97 μm	16 μm	1 ug/mm2	Wedge
Biomatrix	137 μm		15.6 μg/mm	
Endeavor	91 μm	5.3 μm	10 ug/mm	Oval
Xience	81 μm	7.8 μm	~6 ug/mm	Square
CardioMind	67 μm	8 μm	6.3 ug/mm	Oval

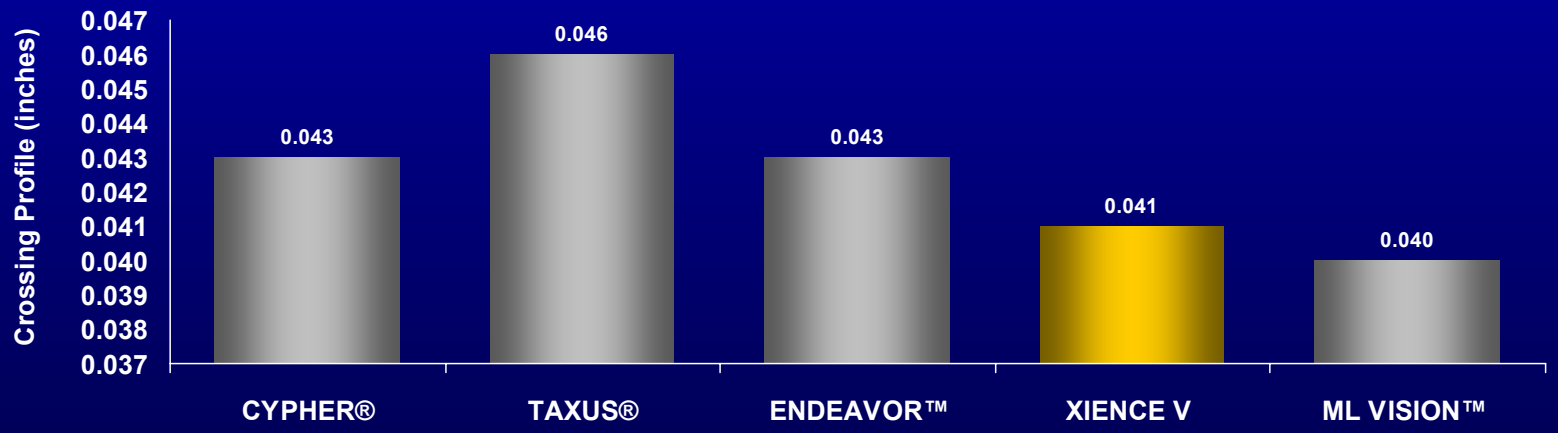
XIENCE V DES Crossing Profile

CRIMPED SYSTEM

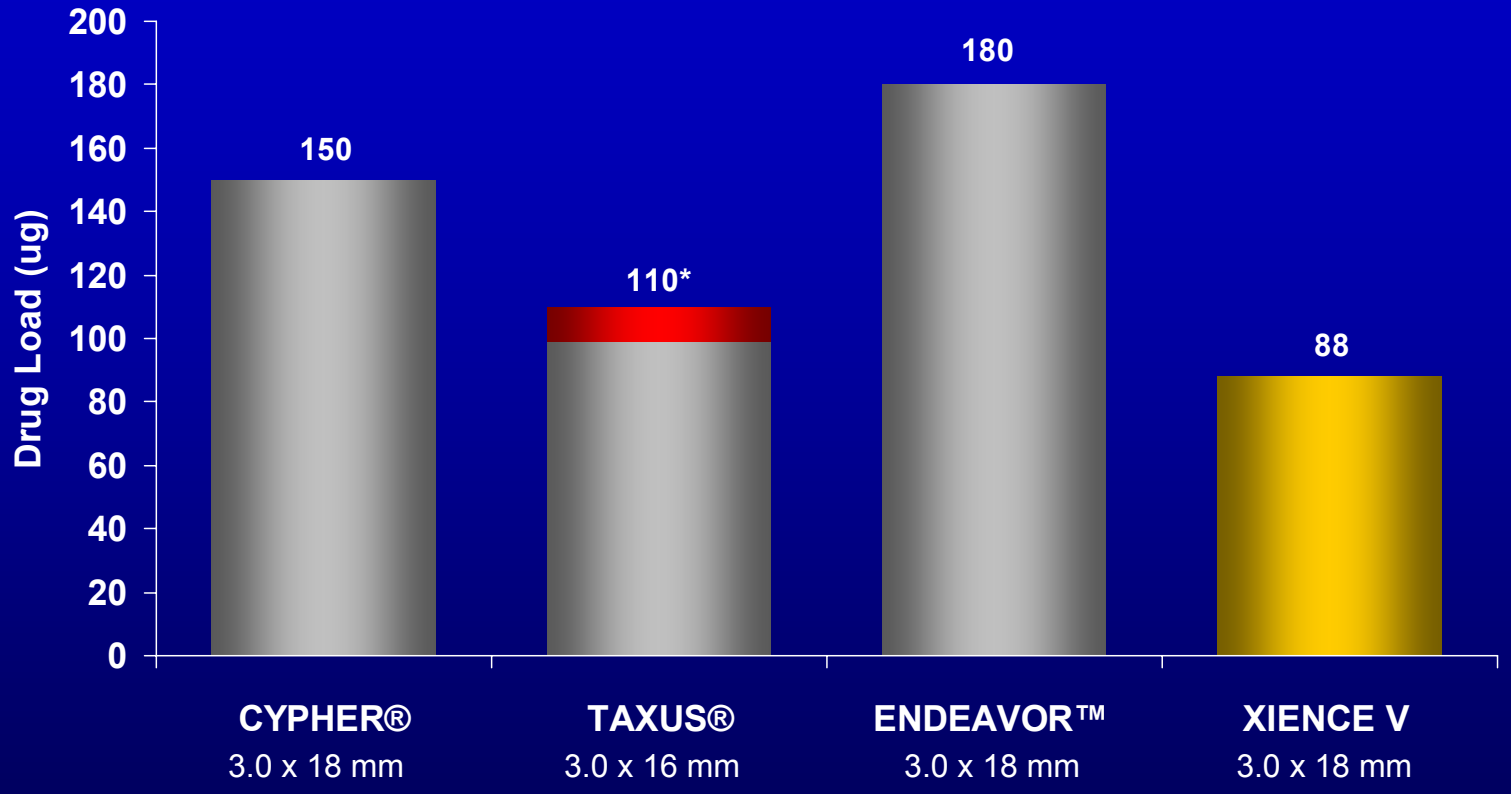
TIP ENTRY PROFILE



Excellent Stent Retention



XIENCE V: Drug Load



Decision-Making in a Multi-DES Environment

We use published and peer-reviewed evidence, peer and personal opinion

- Patient
  - Age – frailty, life expectancy
  - Presentation – acute MI, high risk ACS
  - Comorbidities – DM, CRF, surgical needs, bleeding
  - Socio-economic – compliance with DAPT, remote location
- Vessel
  - Left Main, prox LAD, multivessel, small vessel, graft
- Lesion
  - Long lesion, bifurcation, ostial, thrombus, angulated
- Laboratory Factors
  - Contractural agreements, commercial and research relationships

The Big Four

- All have strong pre clinical programs
- All have well constructed, large scale clinical trial programs
  - Met surrogate endpoints
  - Met hard objective single and composite clinical endpoints
  - Established short to medium term clinical safety
- All are widely accepted and used in front line clinical applications almost globally

Current XIENCE V Clinical Trials

	SPIRIT FIRST	SPIRIT II	SPIRIT III	SPIRIT IV	SPIRIT V	XIENCE V SPIRIT WOMEN	XIENCE V USA	XIENCE V India
	4 year F/U	3 year F/U	2 year F/U	Enrollment Complete	Enrollment Complete	Enrolling	Enrollment Complete	Enrolling
	Safety and Performance	Clinical Support for CE Launch	U.S. and Japan Approval	U.S. Continued Access	Post CE Mark Approval International	Post CE Mark Approval International	U.S. Post Approval	India Post Approval
	Europe N=60	International N=300	U.S.: 65 sites Japan: 12 sites N=1380 (1,292/88)	Expanded Enrollment: N=3,690	N=3,000 100 sites Registry N=2,700 Diabetic study N=300	N=2,000 100 sites Registry N=1,550 (1499* pts enrolled) Randomized arm vs Cypher N=450 (107* pts enrolled)	N=5065	N=1000 Enrolled pts = 932*

* As Mar. 2, 2009

Anticipated Total # Patients = 14,000

Practical "Real World" Application of Evidence in a Multi-DES Environment

- Work horse lesion with or without caveats
- Complex lesion
  - Patient
    - Age – frailty, life expectancy
    - Presentation – acute MI, high risk ACS
    - Comorbidities – DM, CRF, surgical needs, bleeding
    - Socio-economic – compliance with DAPT, remote location
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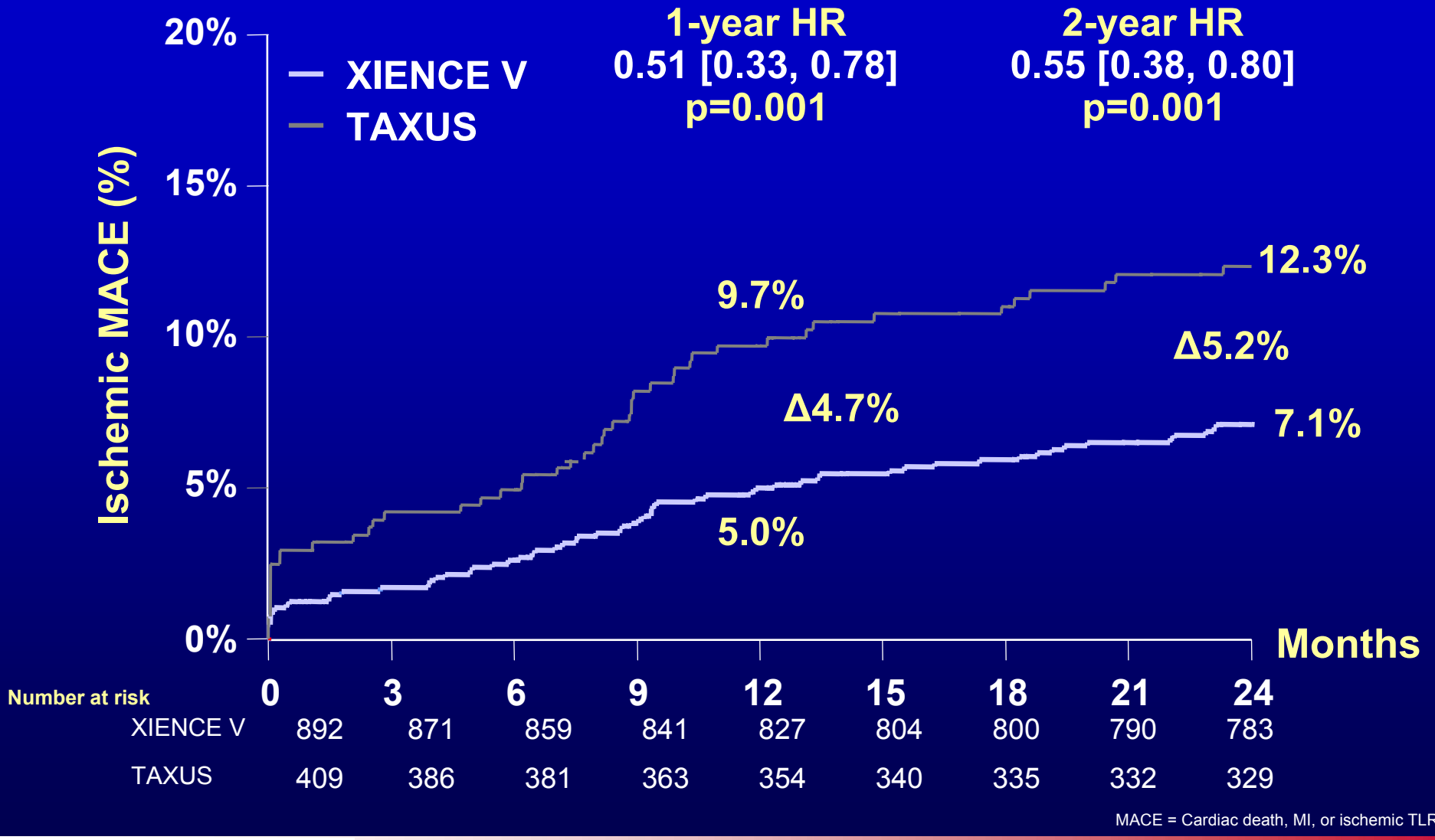
SPIRIT II & III Meta-Analysis

Ischemic MACE Through Two Years

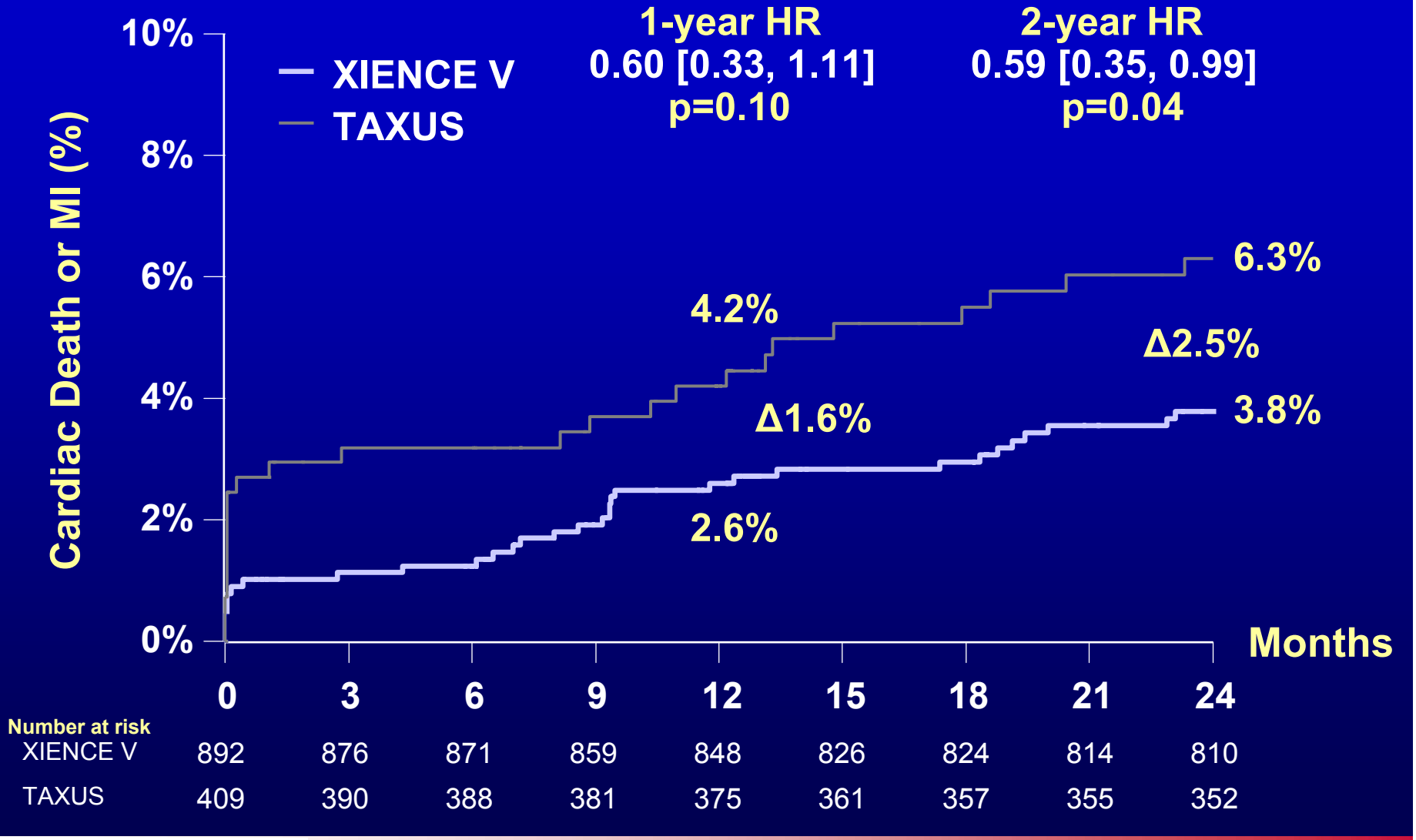


MACE = Cardiac death, MI, or ischemic TLR

SOURCE: Gregg Stone, SPIRIT II & III Meta Analysis Two Year Results, TCT 2008

SPIRIT II & III Meta-Analysis

Cardiac Death and MI Through Two Years



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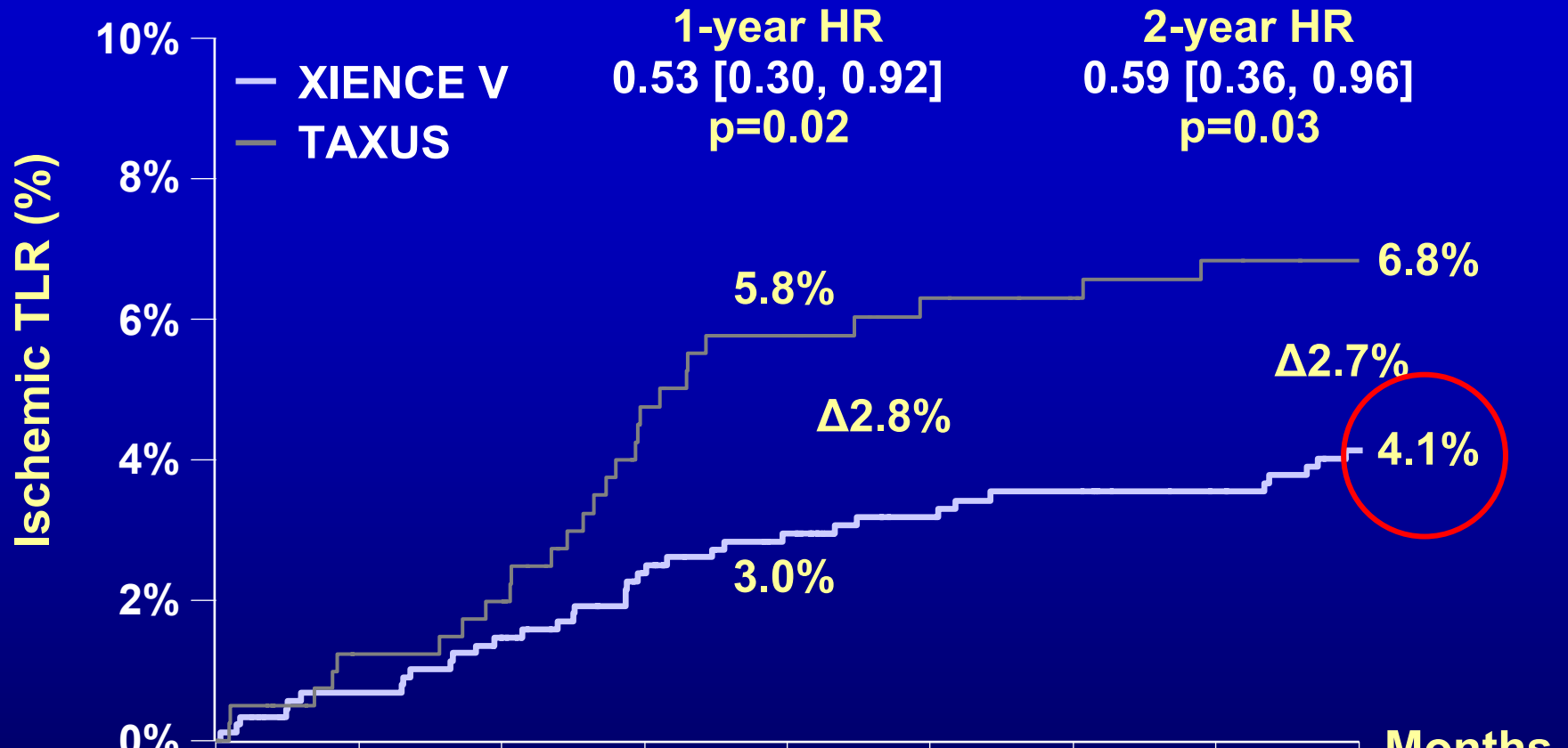
SOURCE: Gregg Stone, SPIRIT II & III Meta Analysis Two Year Results, TCT 2008

Angioplasty Summit-TCT Asia Soeul April 2009

SPIRIT II & III Meta-Analysis

Ischemic TLR Through Two Years



Number at risk	0	3	6	9	12	15	18	21	24
XIENCE V	892	880	869	852	840	819	816	808	801
TAXUS	409	397	392	375	366	354	349	348	346

MONASHHEART

SOURCE: Gregg Stone, SPIRIT II & III Meta Analysis Two Year Results, TCT 2008

Angioplasty Summit-TCT Asia Soeul April 2009

Practical Real World Application of Evidencein a Multi-DES Environment

- Work horse lesion with caveats
- Complex
  - Patient
    - Age – frailty, life expectancy
    - Presentation – acute MI, high risk ACS
    - Comorbidities – DM, CRF, surgical needs, bleeding
    - Socio-economic – compliance with DAPT, remote location
  - Vessel
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  - Lesion
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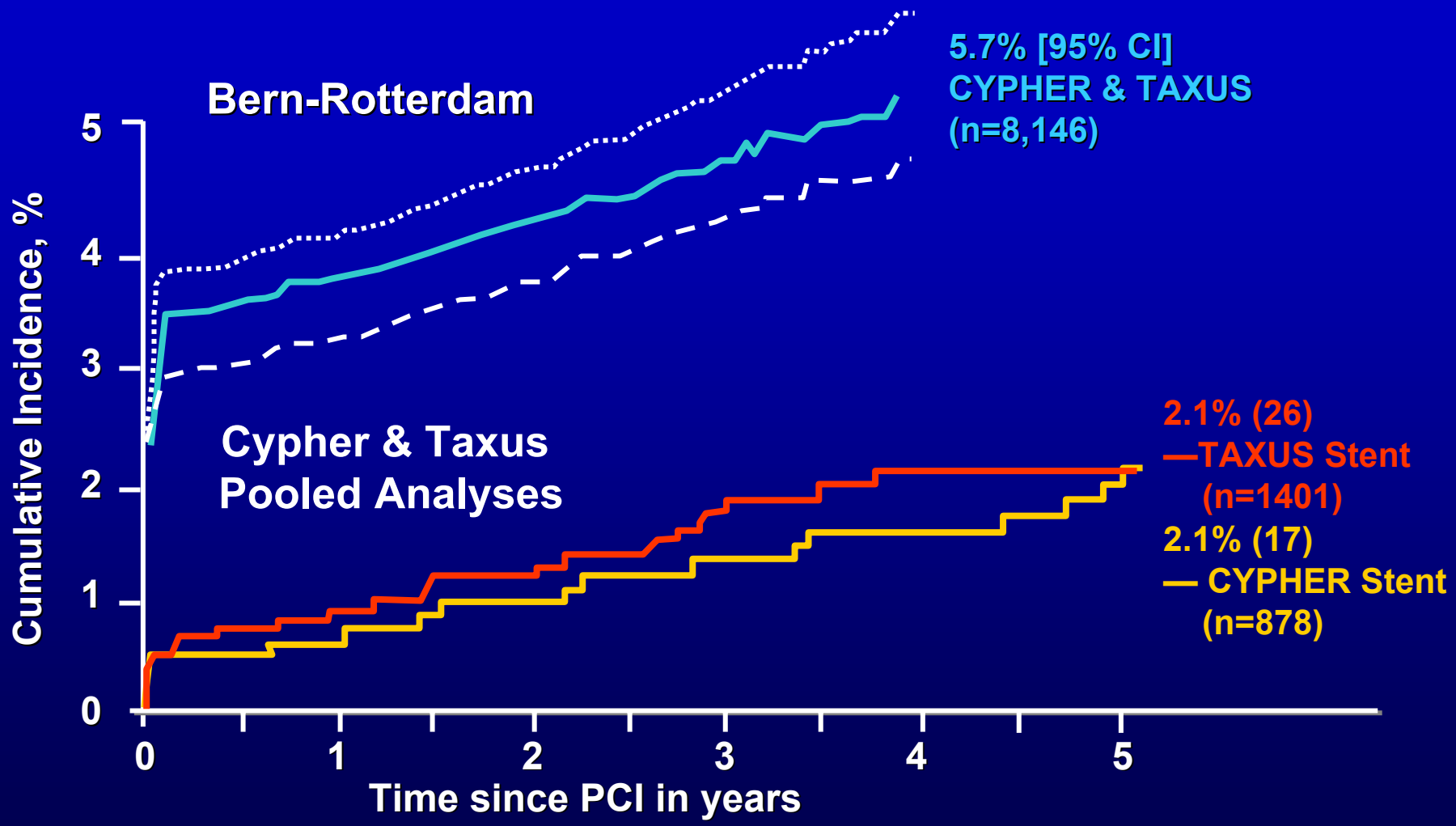
Very Late Stent Thrombosis

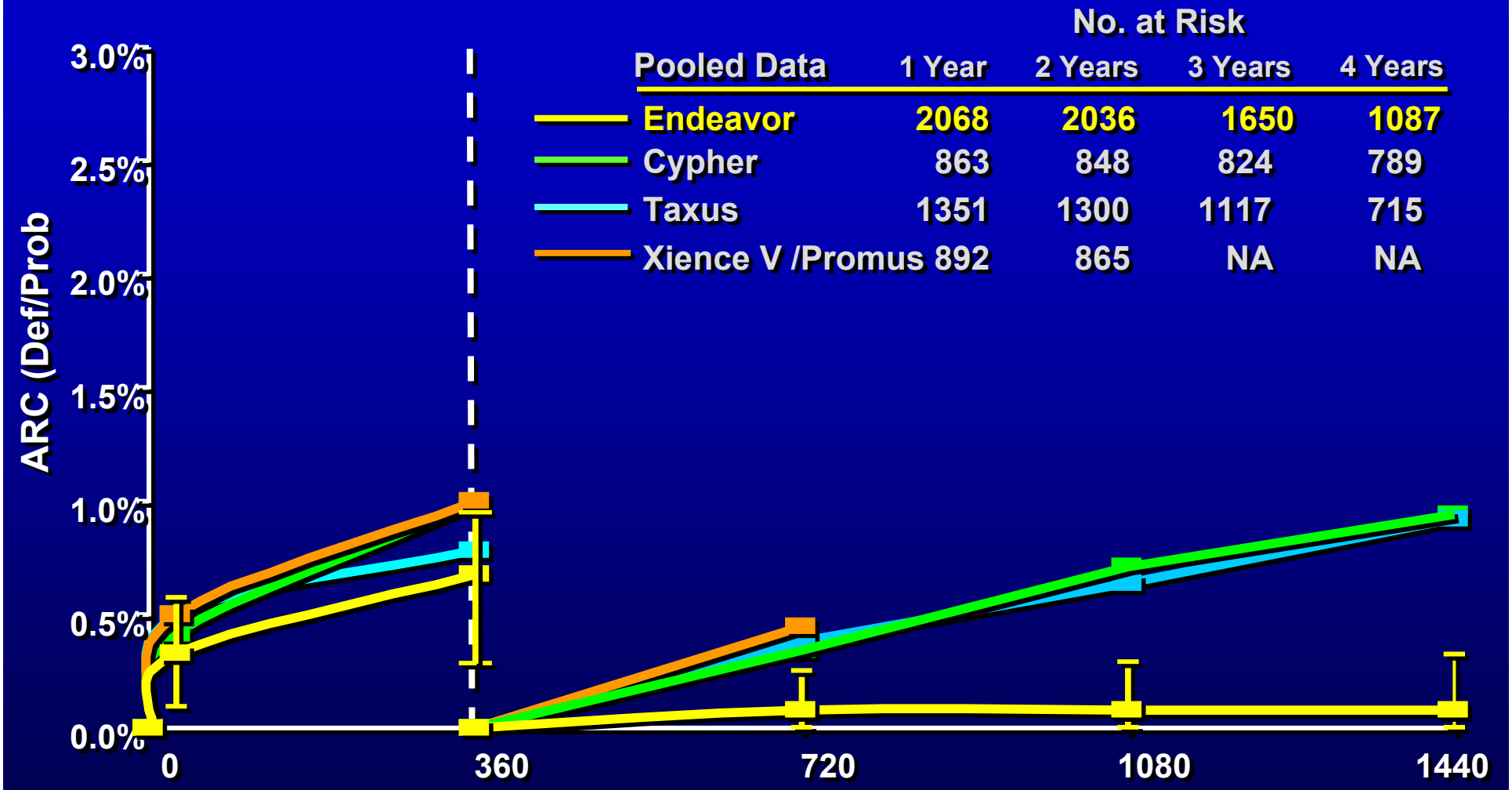
Cumulative Incidence of 1st Generation DES to 4 and 5 yrs



Wenaweser et al; J Am Coll Cardiol 2008;52:1134-40
Kirtane et al; TCT2007: On--Label CYPHER and
TAXUS Randomized Trials with 5--Year Follow

DES In Perspective: VLST

ARC Def/Prob ST Landmark Analysis



As presented by Ian Meredith MD at PCR 2008
1. Mauri et al. TCT 2008.
2. Mauri L et al. *N Engl J Med*. 2007;356:1020-1029.
3. Serruys PW et al. *ACC* 2008
3. Stone GW et al. *PCR* 2008.

Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) trials are not adequately powered to fully characterize. This is a post-hoc analysis

Practical Application of Evidence in a Multi-DES Environment

- Work horse lesion with or without caveats
- Complex lesions
  - Patient
    - Age – frailty, life expectancy
    - Presentation – acute MI, high risk ACS
    - Comorbidities – DM, CRF, surgical needs, bleeding
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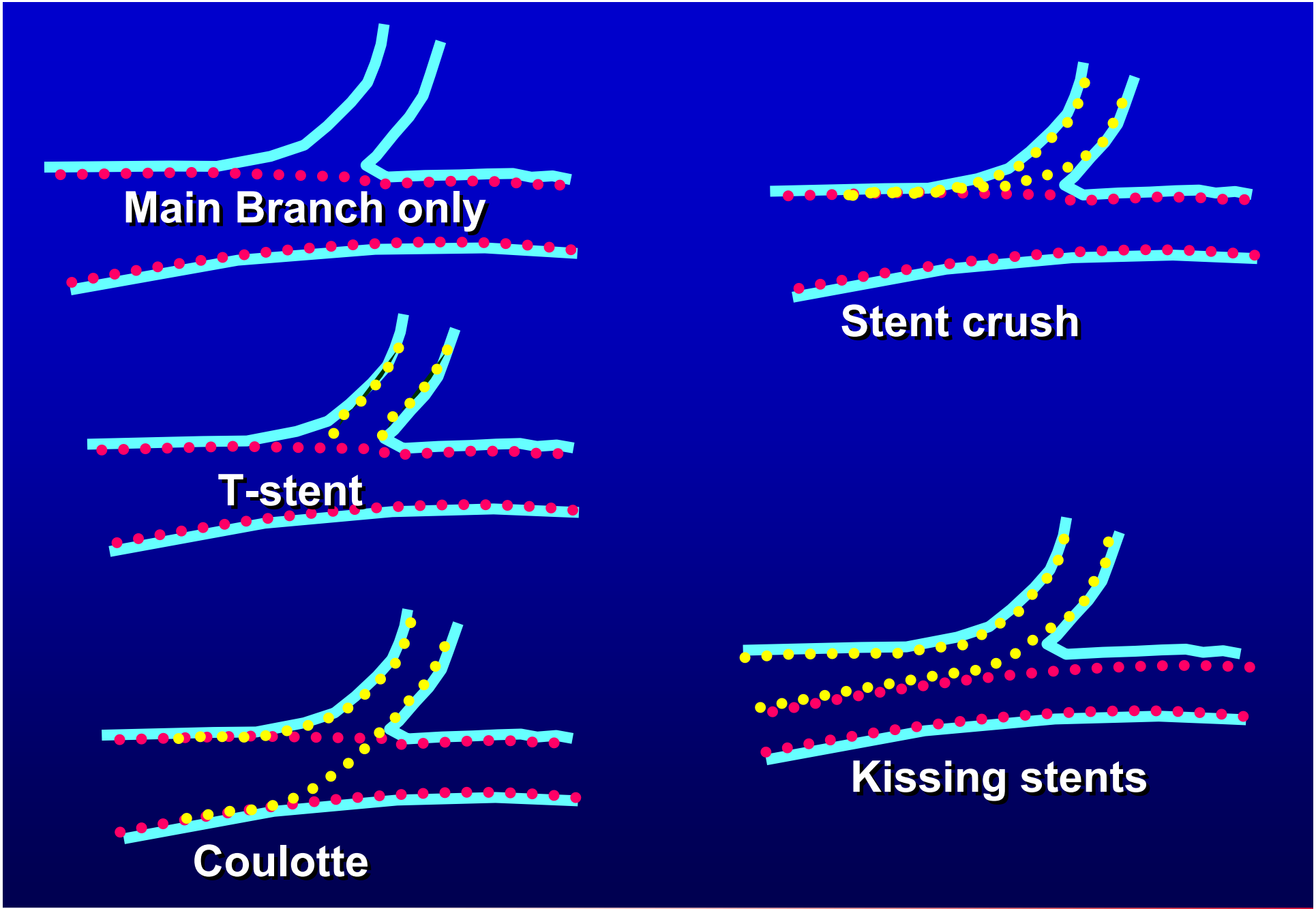
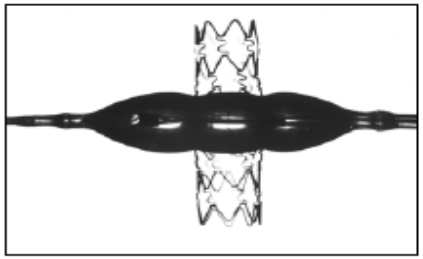
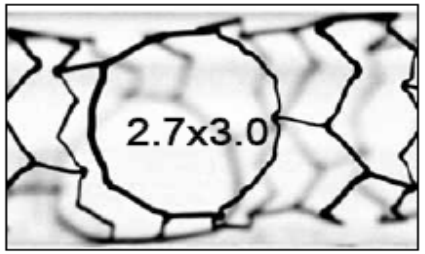

Main Branch only
Stent crush
T-stent
Kissing stents
Coulotte

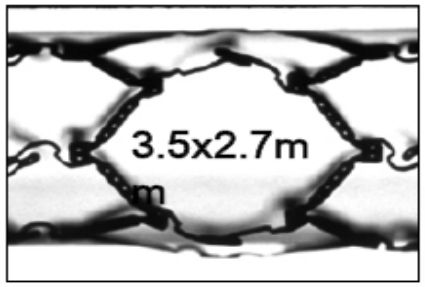
Side Branch Expansion Comparison

Conventional photos and Cell Size after SB Dilatation with a 4mm Balloon

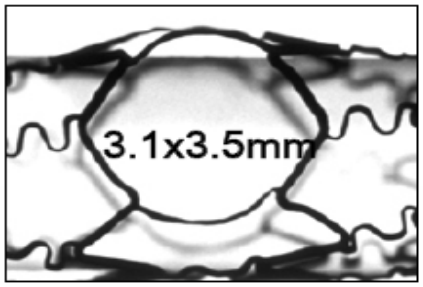




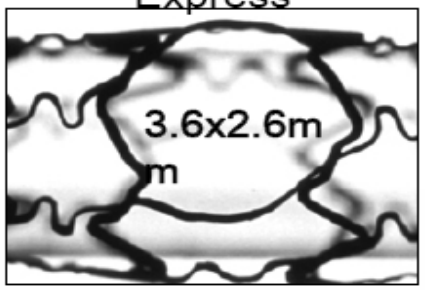
Express



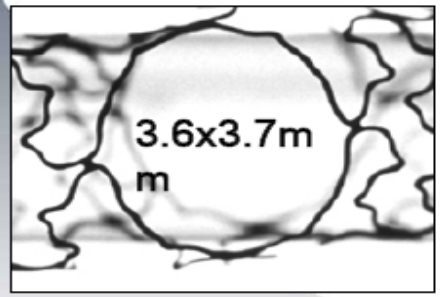
CoStar



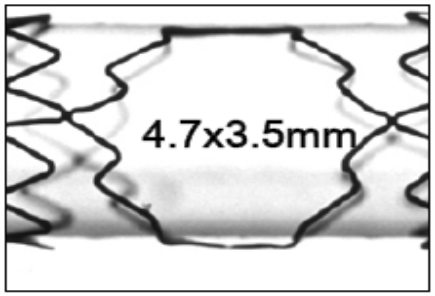
Bx Velocity



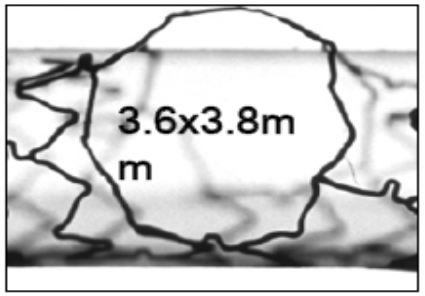
Select



Liberte



Driver



Vision

Courtesy of J. Ormiston

TCT2007

CARDIOVASCULAR RESEARCH FOUNDATION

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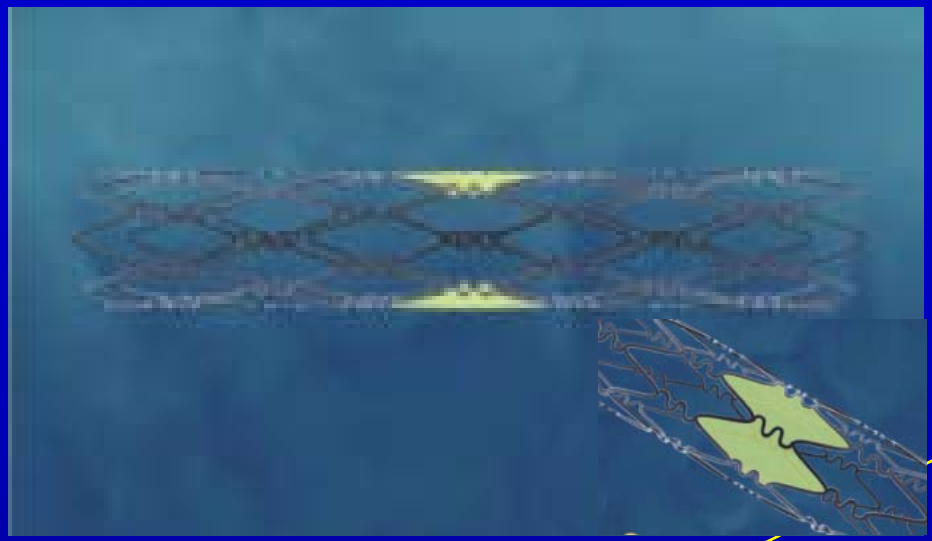
Source; CRTOnline "Simple and Complex Bifurcation Lesions; Classification, Single and Dual Stent Options, Clinical Outcomes, and a Simple Treatment Algorithm Y. Louvard

Open Cell Design

Closed Cell Design



Practical Application of Evidence in a Multi-DES Environment

- Work horse lesion with or without caveats
- Complex lesions
  - AMI

Pasceri Meta Analysis of Clinical Trials of DES compared to BMS in AMI

	No	% F Sex	Mean Age	DES	Angio F/U	IIb/IIIa	LAD culprit	Rescue PCI	F/U mths	MACE Endpoints Death/ MI/TVR
Pasceri	65	18	60	Cypher	100%	90%	50%	18%	12	21.7%
STRATEGY	175	27	63	Cypher	90%	100%	45%	No	8	25%
PASSION	605	24	61	Taxus Express	No	27%	45%	No	12	10.9%
TYPHOON	712	22	59	Cypher	26%	72%	50%	No	12	10.9%
SESAMI	320	19	61	Cypher	52%	NA	50%	18%	12	11.8%
HAAMU-Stent	164	28	63	Taxus Express	88%	100%	44%	45%	12	15.2%
MISSION	316	22	59	Cypher	82%	100%	55%	No	12	18.6%

HORIZONS AMI

Harmonizing Outcomes with Revascularization and Stents in AMI

≥3400* pts with STEMI with symptom onset ≤12 hours

Aspirin, thienopyridine

R 1:1

- UFH + GP IIb/IIIa inhibitor (abciximab or eptifibatide)
- Bivalirudin monotherapy (± provisional GP IIb/IIIa)

Emergent angiography, followed by triage to…

CABG – Primary PCI – Medical Rx

3000 pts eligible for stent randomization

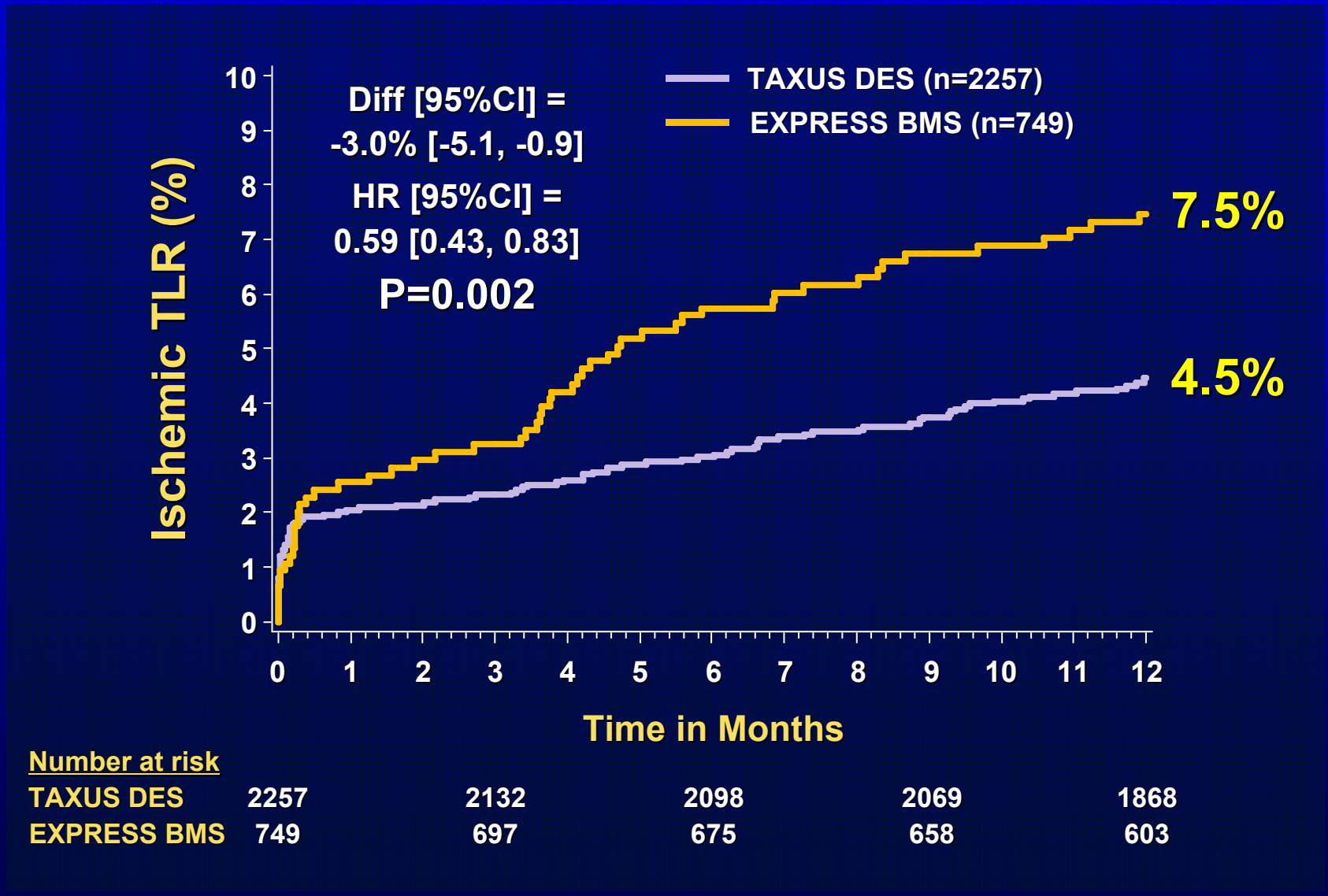
R 1:3

- Bare metal stent
- TAXUS paclitaxel-eluting stent

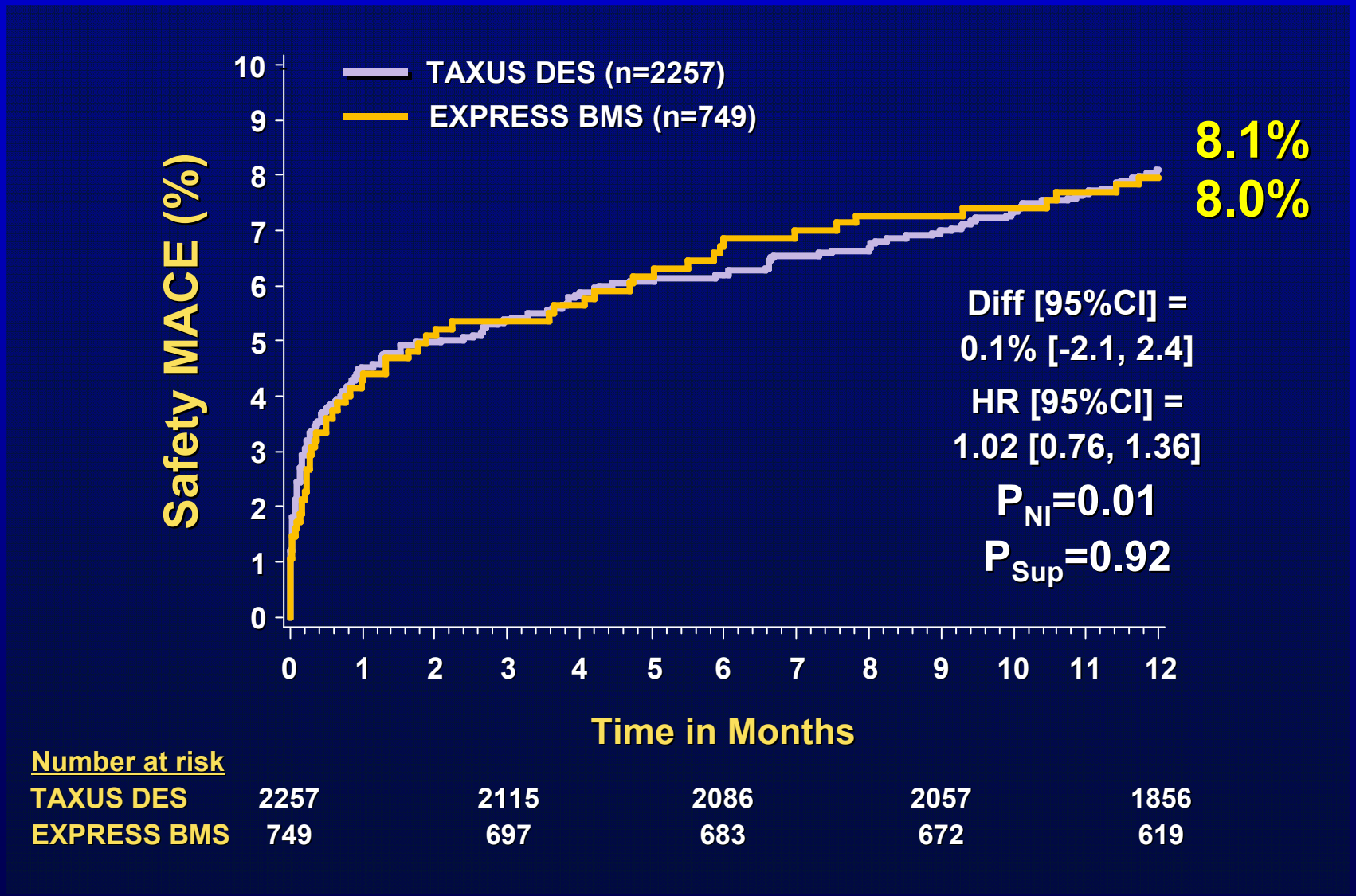
Clinical FU at 30 days, 6 months, 1 year, and then yearly through 5 years

*To rand 3000 stent pts

Primary Efficacy Endpoint: Ischemic TLR

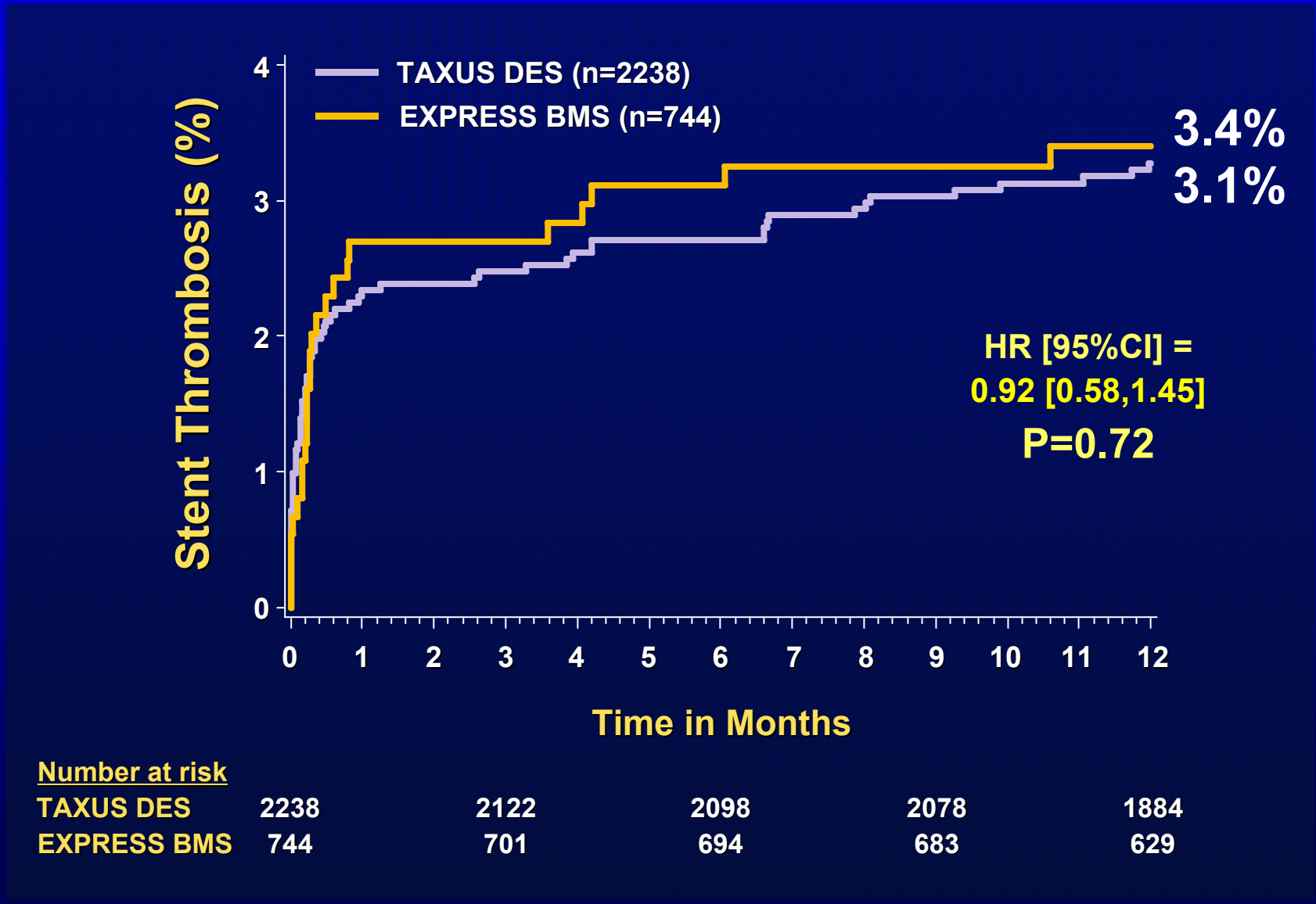


Primary Safety Endpoint: Safety MACE*



* Safety MACE = death, reinfarction, stroke, or stent thrombosis

Stent Thrombosis (ARC Definite or Probable)



Number at risk					
TAXUS DES	2238	2122	2098	2078	1884
EXPRESS BMS	744	701	694	683	629

Where to next ?

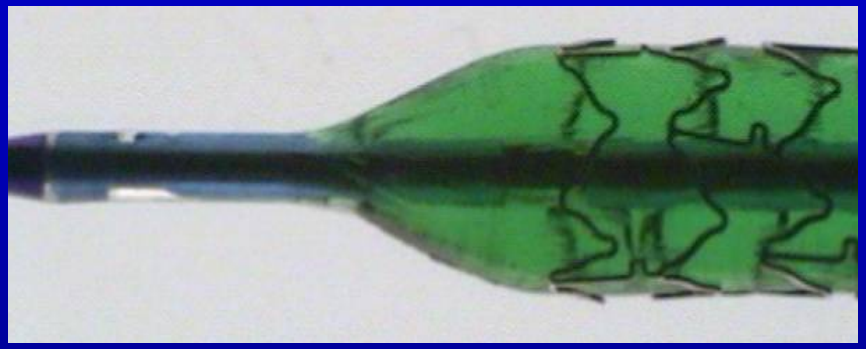
XIENCE Prime

- **Built upon the XIENCE V body of clinical evidence**
- **Proven drug and polymer from XIENCE V**
- **Outstanding Acute Performance**
  - **New stent delivery system for more responsive catheter performance**
  - **Enhanced stent design** with connecting link and ring geometry for improved deliverability and conformability**
  - **Short balloon tapers for safe deployment**
  - **Higher RBP for confident placement**
- **Full matrix of lengths and diameters**
  - **46 sizes vs. 36 for XIENCE V**

Tests performed by and data on file at Abbott Vascular.

A Commitment to Innovation
Redesigned Stent Delivery System

XIENCE V



XIENCE PRIME

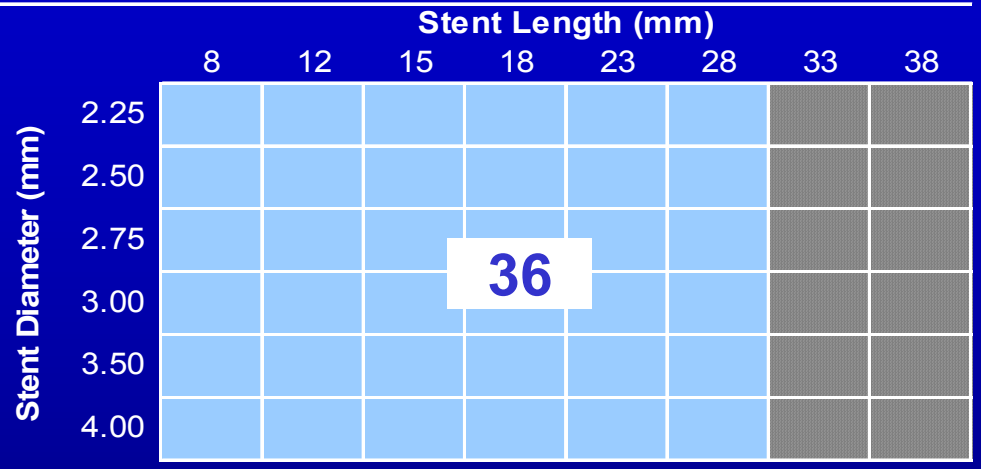
Photographs taken by and on file at Abbott Vascular.

The SDS is completely redesigned

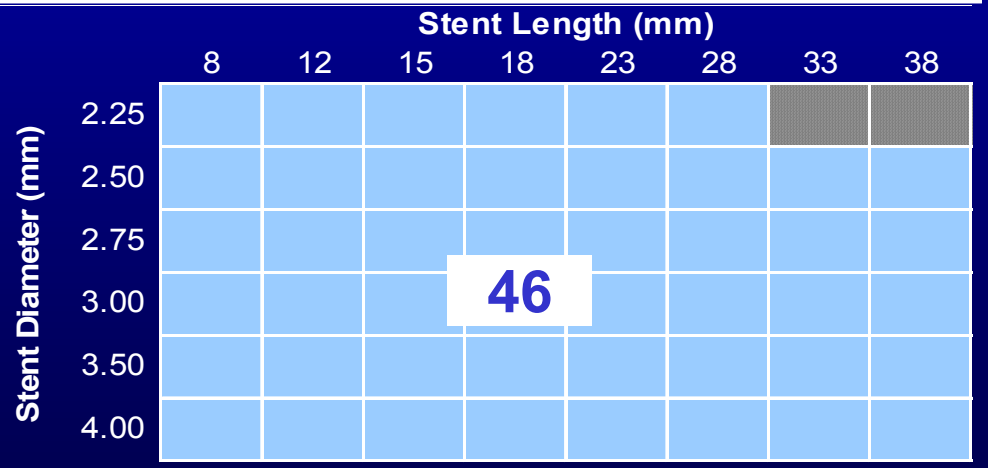
Feature	Benefit
• Redesigned SDS chassis	• Increased pushability and catheter response
• Shorter balloon tapers	• Reduced peri-stent injury
• Higher Rated Burst Pressure	• Permits higher pressure deployment
• Softer tip flexibility	• Easier lesion access
• Significantly lower deflation times	• Faster procedure times

A Commitment to Innovation
Goal: More Available Sizes Than XIENCE V

XIENCE V



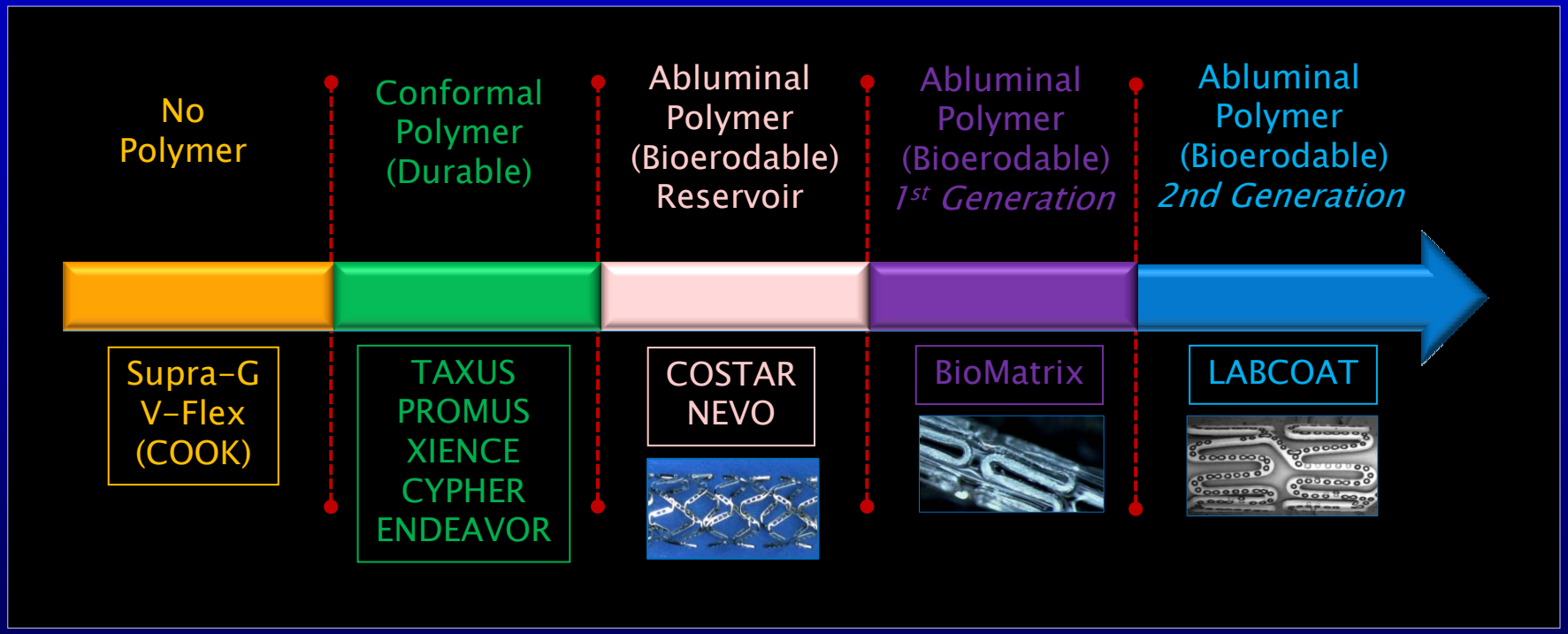
XIENCE PRIME



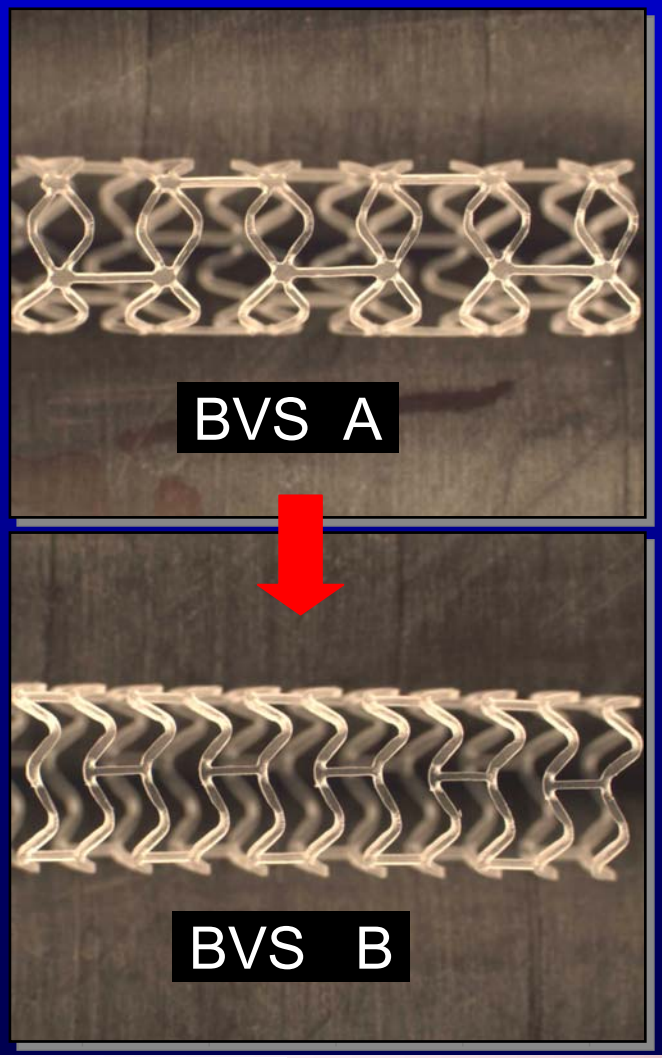
- **Continuous Sizes:**
  2.25 – 4.0 mm diameter
  8 – 28 mm lengths

- **Differences:**
  Longer lengths with XIENCE PRIME (33, 38)

Evolution of Stent Based Drug Delivery



Future Steps
Fully Bioabsorbable Stent Design



- More uniform strut distribution
- More even support of arterial wall
- Lower MCUSA (*maximum circular unsupported surface area*)
- Lower late stent area loss
- Higher radial strength
- Improved stent retention
- Unchanged:
  - Material
  - Strut thickness

Conclusions

- The current generations of DES address some but not all of the DES design issues.
- Overall the programs are characterised by a move to lower profile more flexible stent platforms with lower strut and polymer thickness and potentially more biocompatible polymers.
- The body of comparative data between programs remains small but is expanding.
- Choosing a DES platform in this multi-platiform environment requires the adaptation and translation of the available evidence to patient, vessel, lesion characteristics and the overall clinical setting.