Bioabsorbable and Polymer-Free DES: Current and New Technologies

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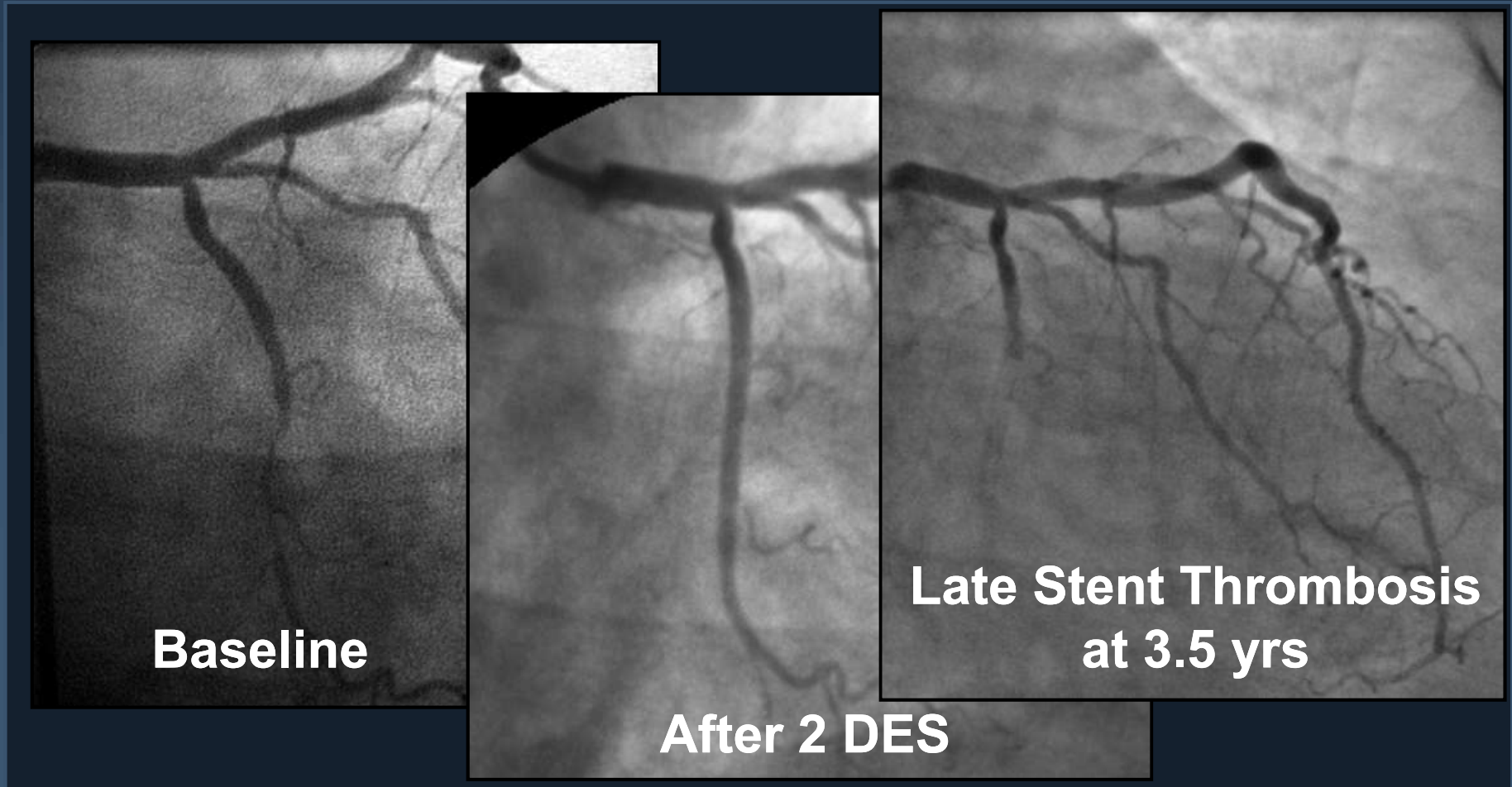
LaST – Late DES Stent Thrombosis After 3 Years



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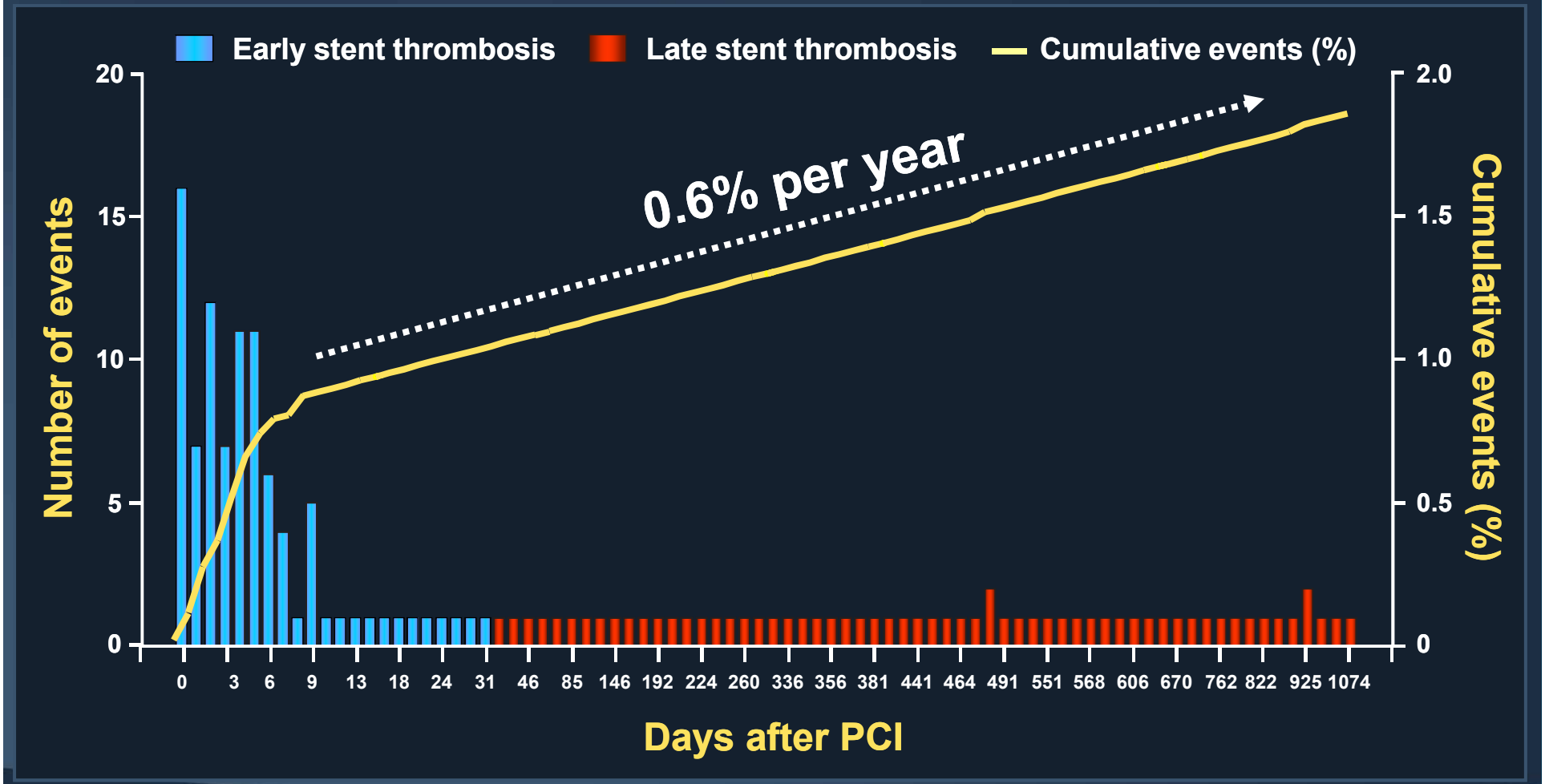
Bern-Rotterdam Experience

8146 pts. treated with SES (n=3823) or PES (n=4323) at 2 academic centers



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Daemon J, et al, *Lancet* 2007;369:667–78

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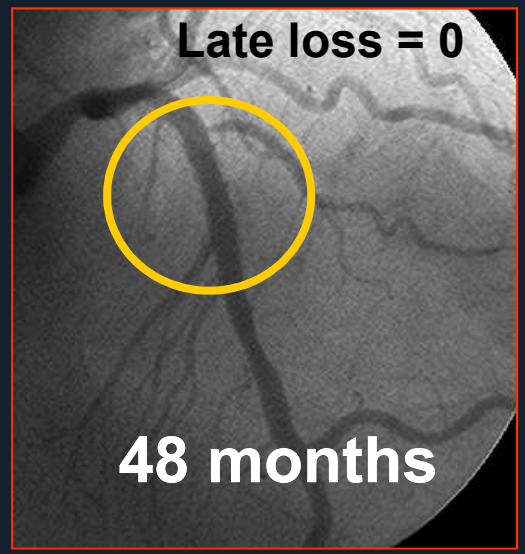
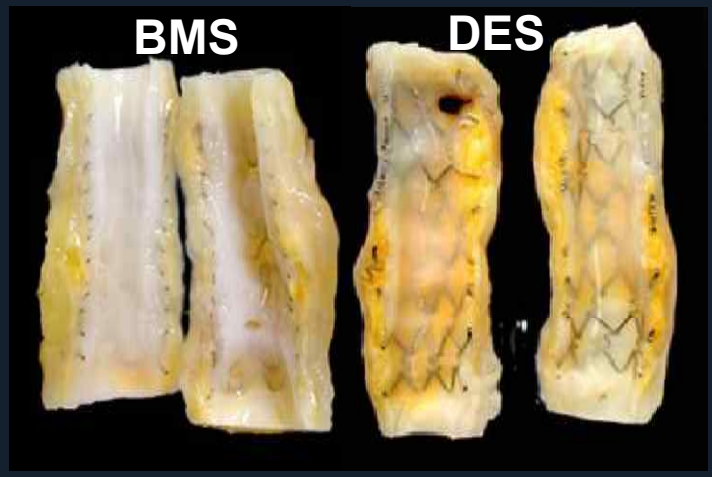
Drug-Eluting Stents

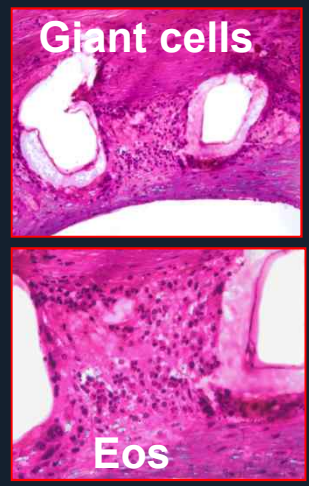
The good, the bad, and the ugly!



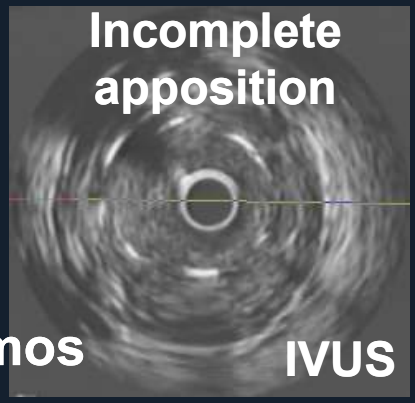


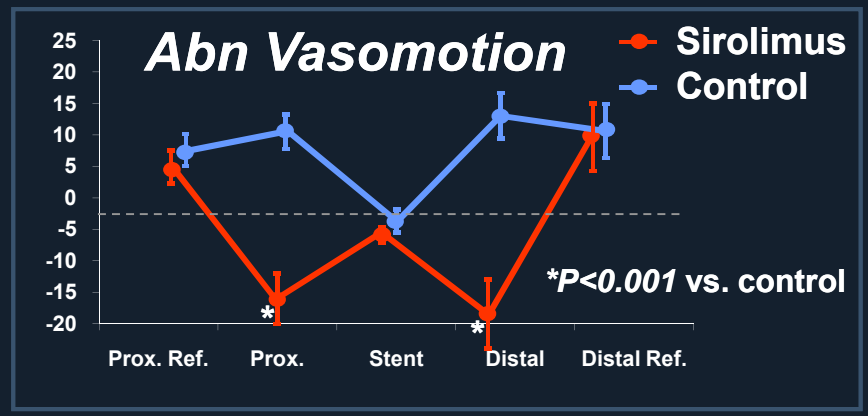
Delayed Healing!

Angioscopy



Inflammation





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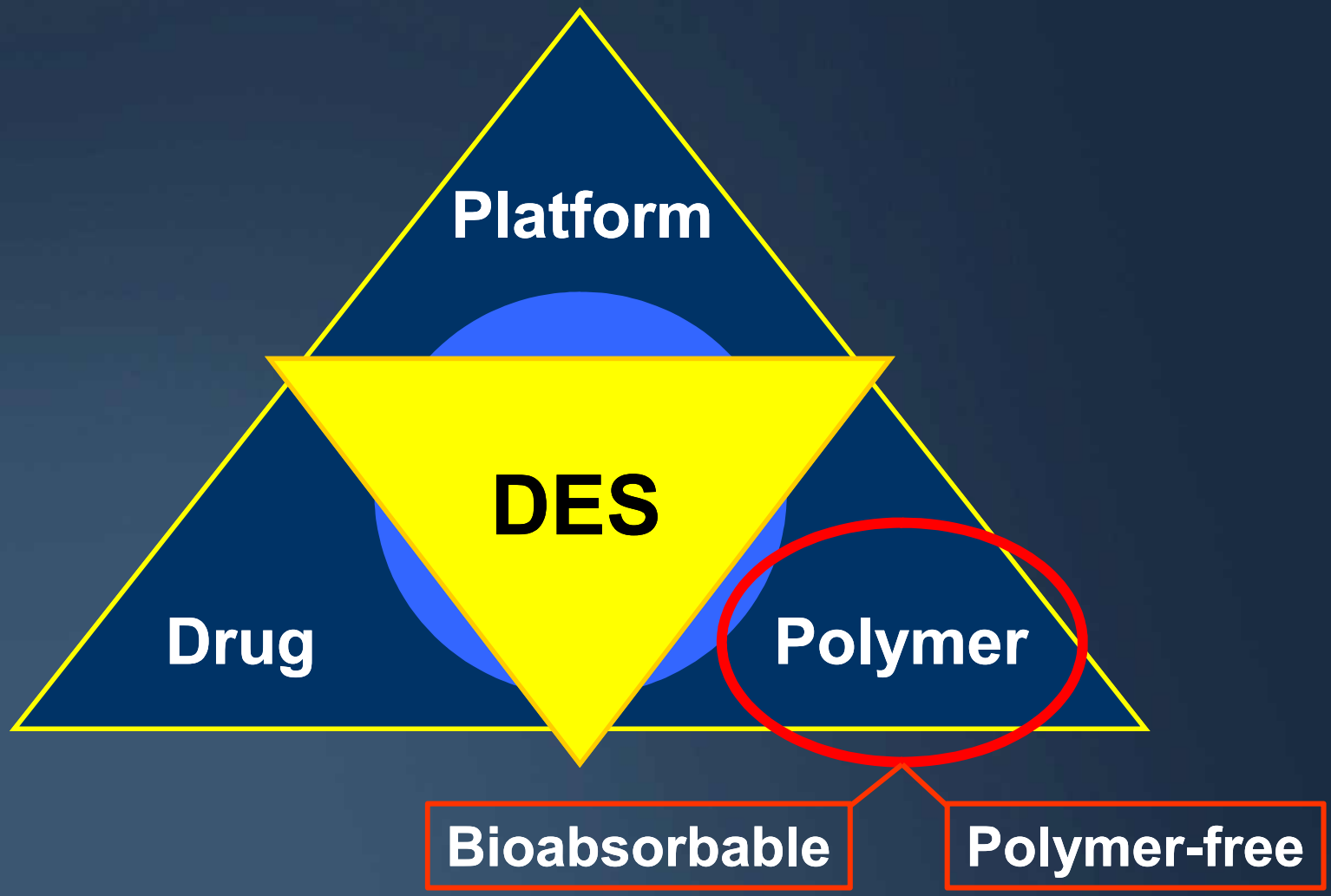
Future DES



Future DES

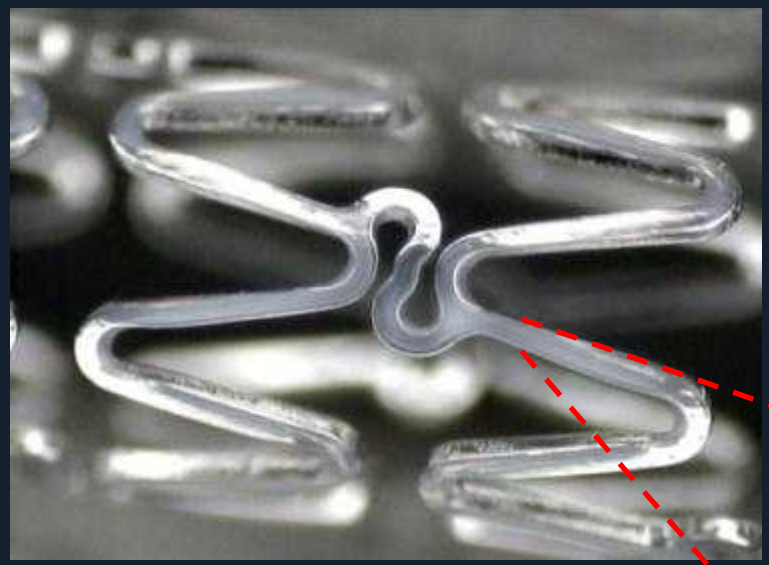
New Drug Carrier Systems…1

- **Bioabsorbable Polymers**
  - **Benefit – reduced polymer burden and bioabsorption should reduce chronic polymer effects (⬆ safety)**
  - **Issues – degradation rates, inflammatory by-products, more complex elution profiles**
  - **Examples: Biosensors (BioMatrix), Translumina (Yukon), Cordis (Nevo), BSC (Jactax), Genous DES**

BioMatrix Stent Platform

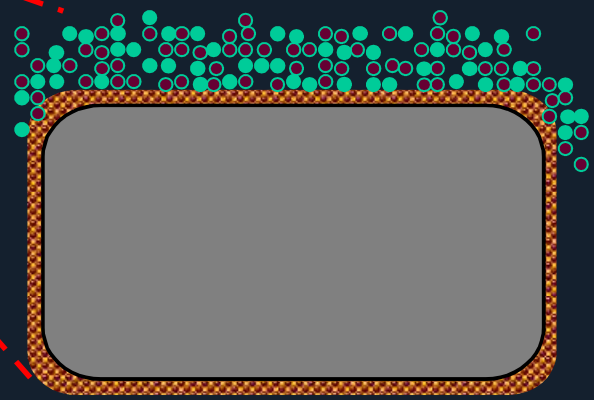
Bioabsorbable Polymer DES

BIOMATRIX®

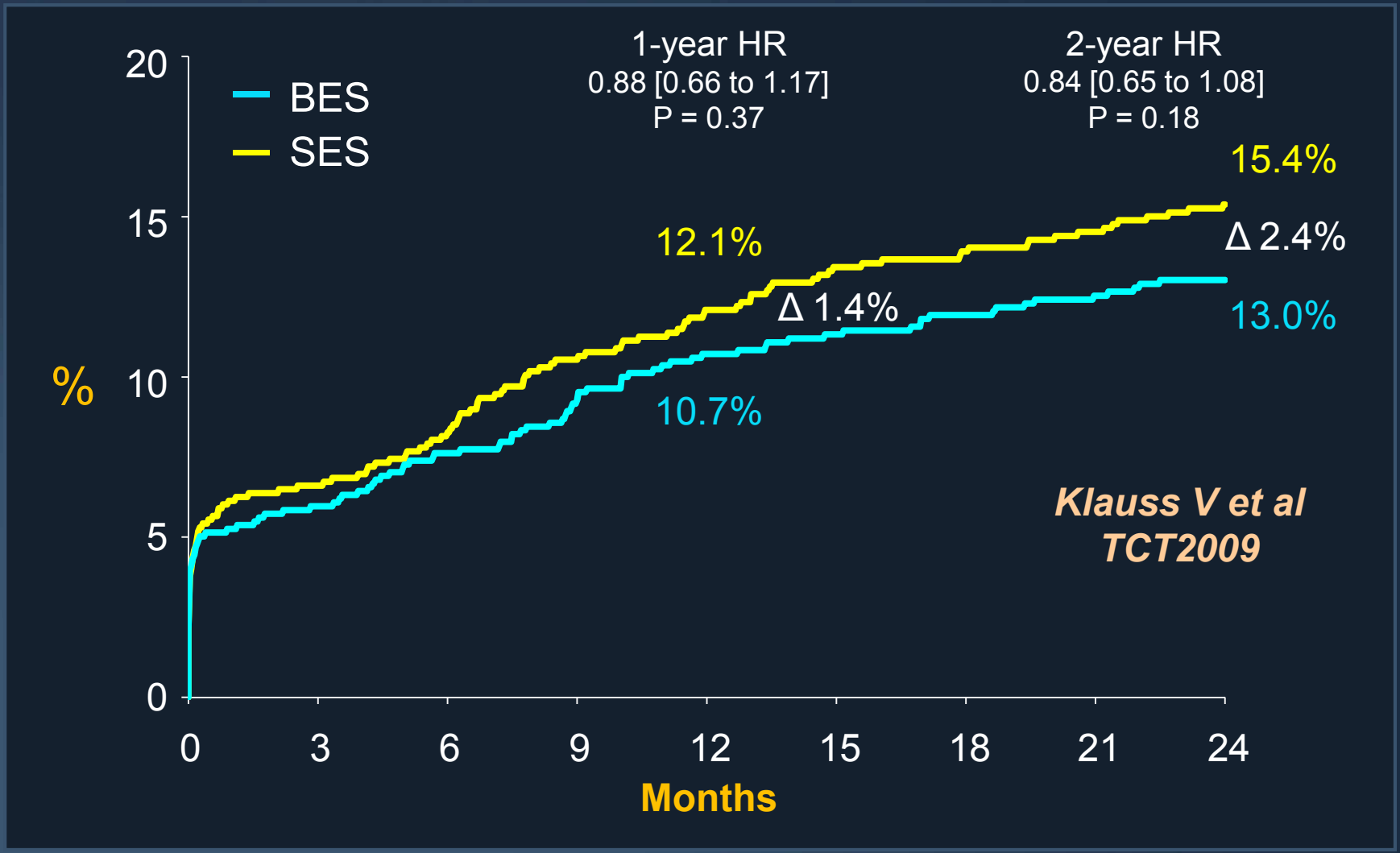


Biodegradable Drug Carrier:

- Biolimus A9 / Poly (Lactic Acid) 50:50 mix
- Abluminal surface only (contacts vessel wall)
- 10 microns coating thickness
- Degrades in 9 months releasing CO_2+ H_2O



LEADERS – MACE (n=1,707)



MACE = Cardiac Death, MI, or Clinically-Indicated TVR

Windecker S et al. Lancet 2008; 372: 1163–73

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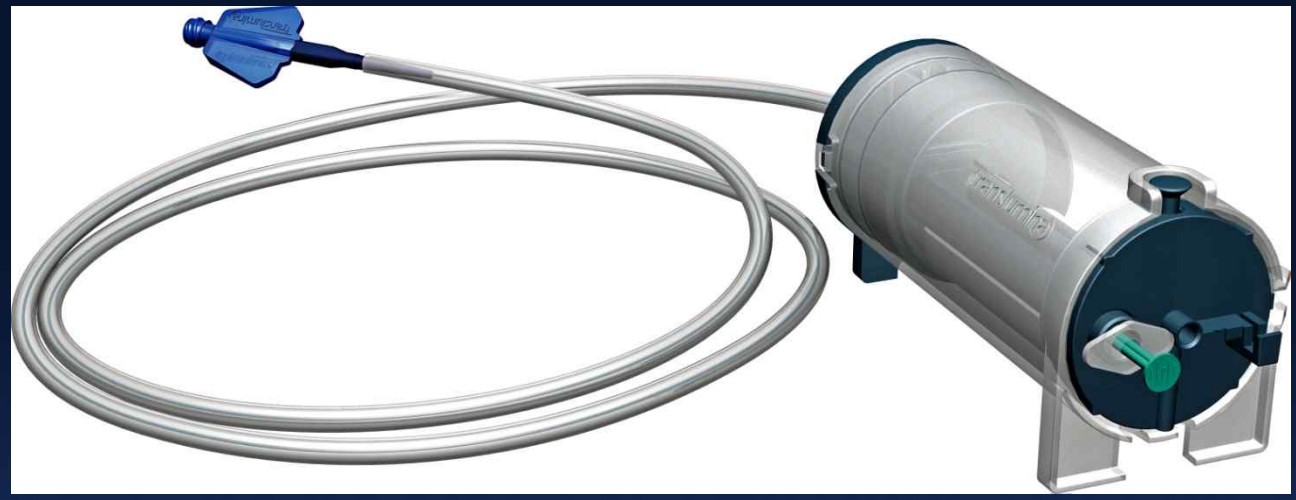
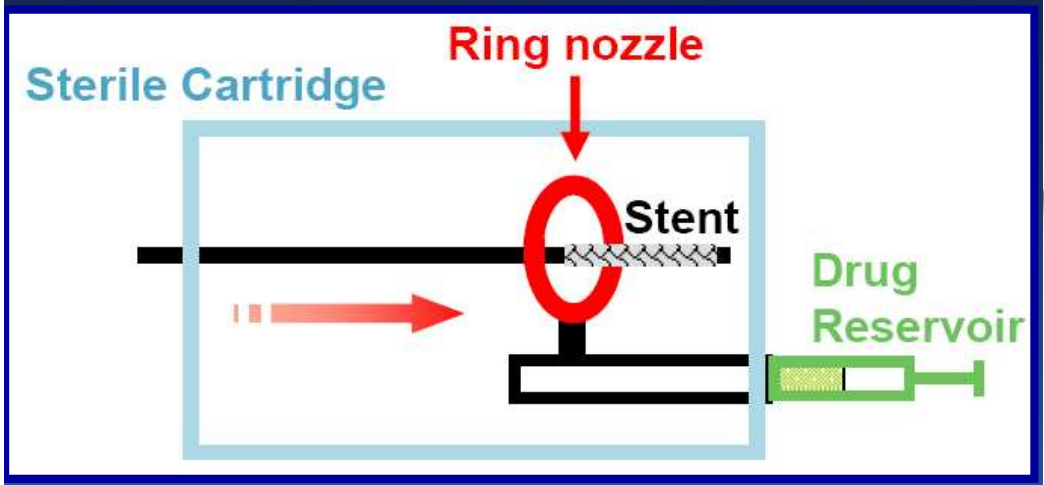
Translumina Coating Technology

Yukon® CC CoCr Stent

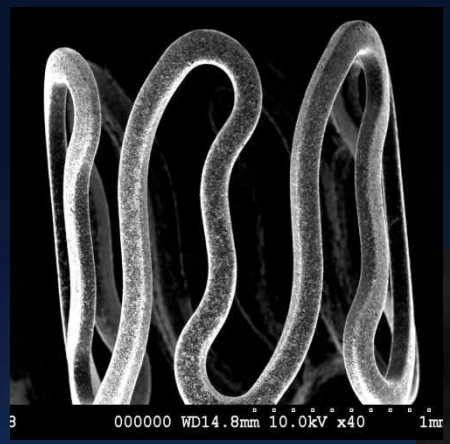


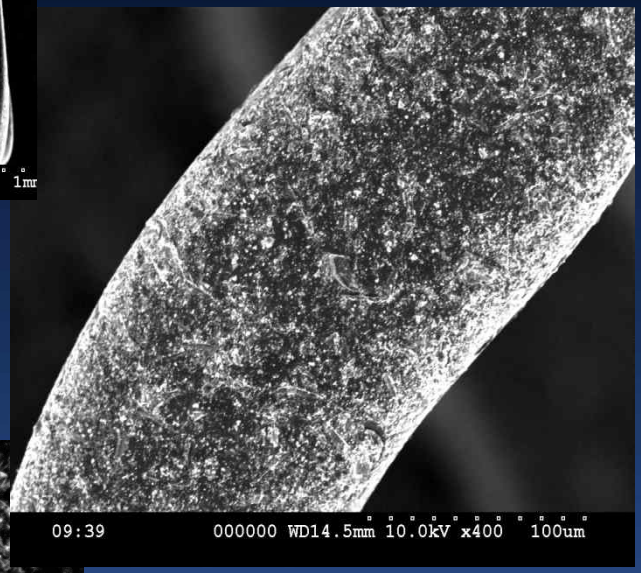


Translumina: Unique Microporous Stent Surface

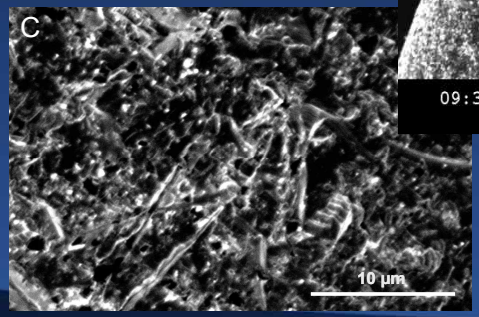
Coating Capacity & Relase Kinetics

Stent Surface

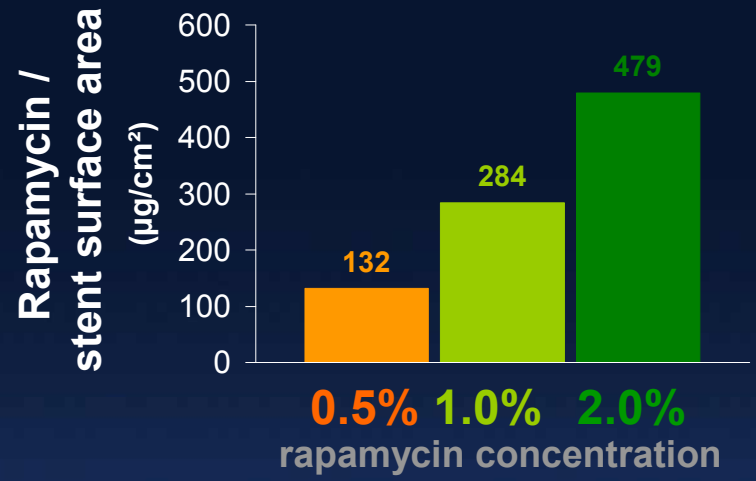




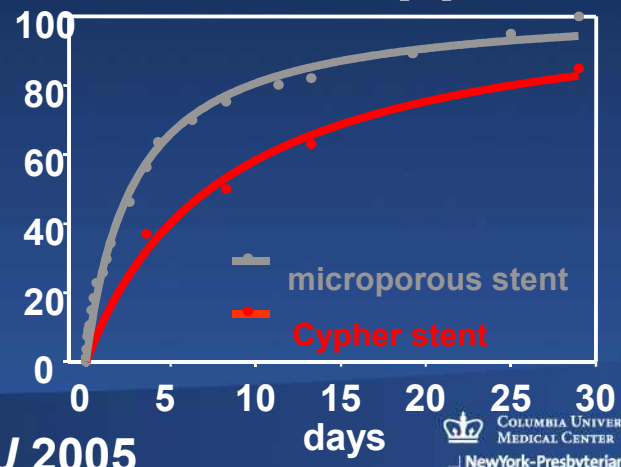
Yukon stent



Coating Capacity



Release Kinetics



J Hausleiter et al. *Eur Heart J* 2005

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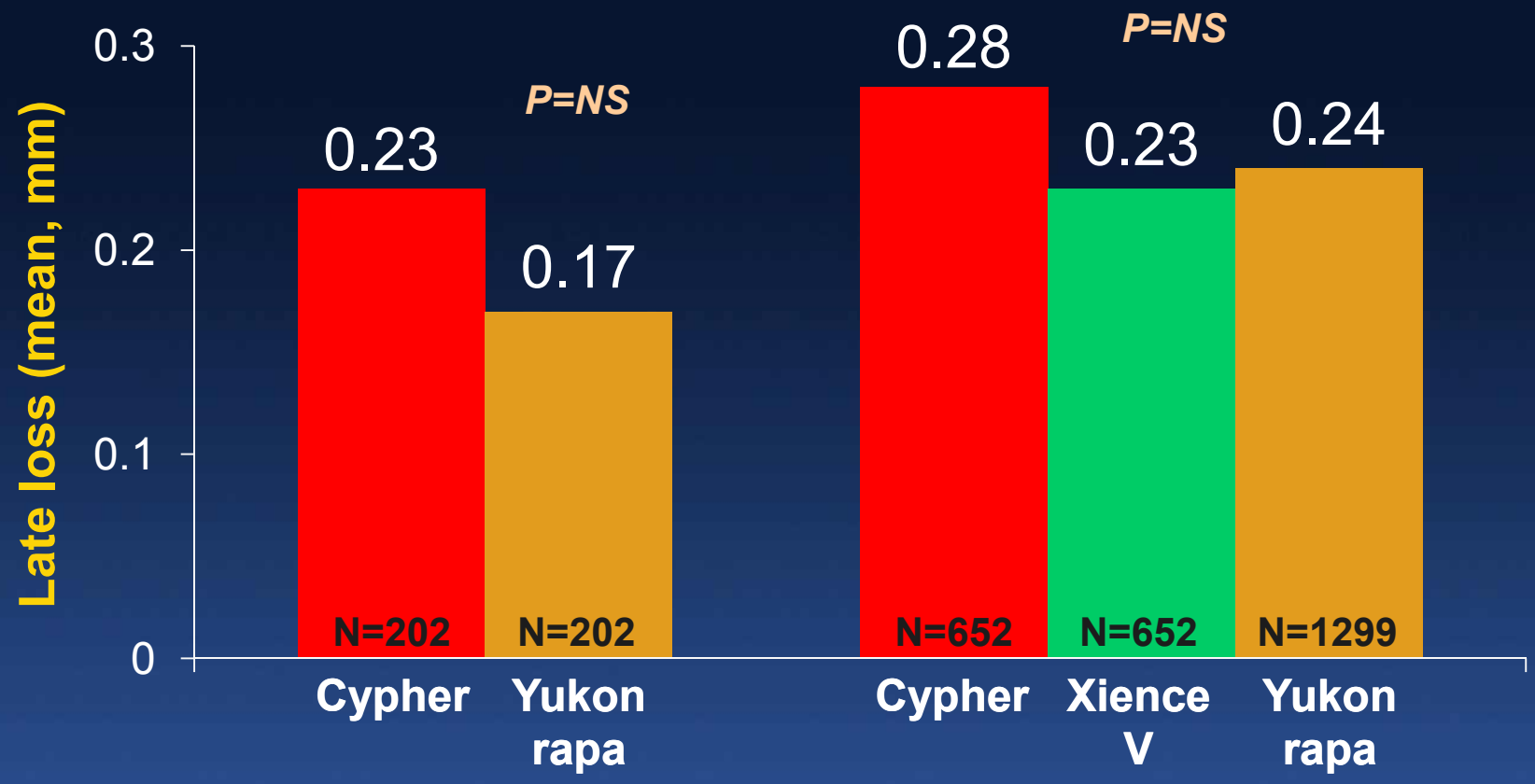
The ISAR-TEST Program

	N	Control stent	Test stent (YUKON)	Primary endpoint
ISAR-TEST 1	450	TAXUS	Rapa polymer-free	In-stent LL 6-8 months
ISAR-TEST 2	1007	CYPHER and ENDEAVOR	Rapa + probucol polymer-free	In-stent LL 6-8 months
ISAR-TEST 3	605	CYPHER	Rapa polymer-free, and Rapa with bioabsorbable polymer	BAR 6-8 months
ISAR-TEST 4	2603	CYPHER and XIENCE V	Rapa with bioabsorbable polymer	TLF 1 year
ISAR-TEST 5 (ongoing)	3000	RESOLUTE	Rapa + probucol polymer-free	MACE 1 year

Rapamycin-eluting Yukon Stent with Bioabsorbable Polymer

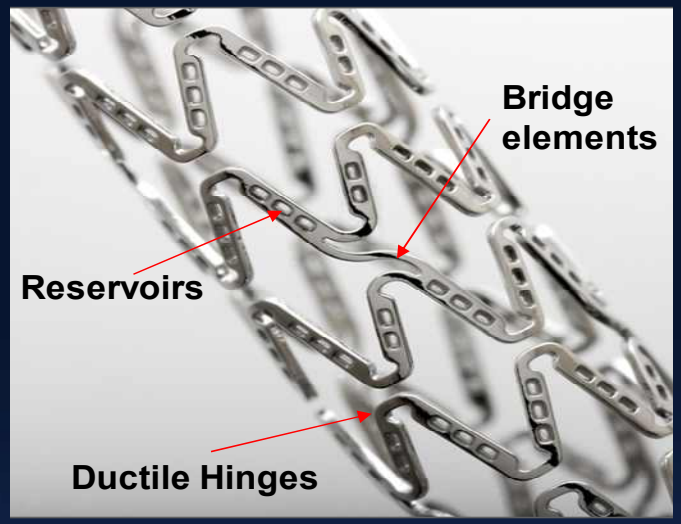
- In-stent late loss at 6-8 months-



ISAR-TEST 3 — J Mehilli et al. Eur Heart J 2008

ISAR-TEST 4 — R Byrne et al. Eur Heart J 2009

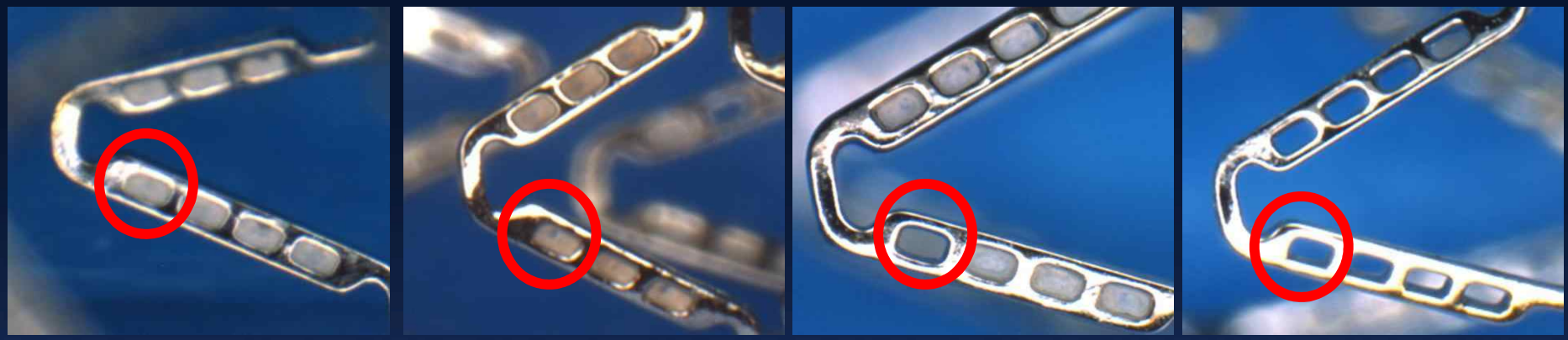
NEVO™ Stent Design



- *Chromium-Cobalt Platform*
  - Flexible, thin struts, open cell design
- *Novel Reservoir Technology*
  - Minimizes polymer - vessel wall contact
- *Biodegradable Polymer*
  - Achieves Cypher-like sirolimus tissue levels
  - Rapid endotheliazation

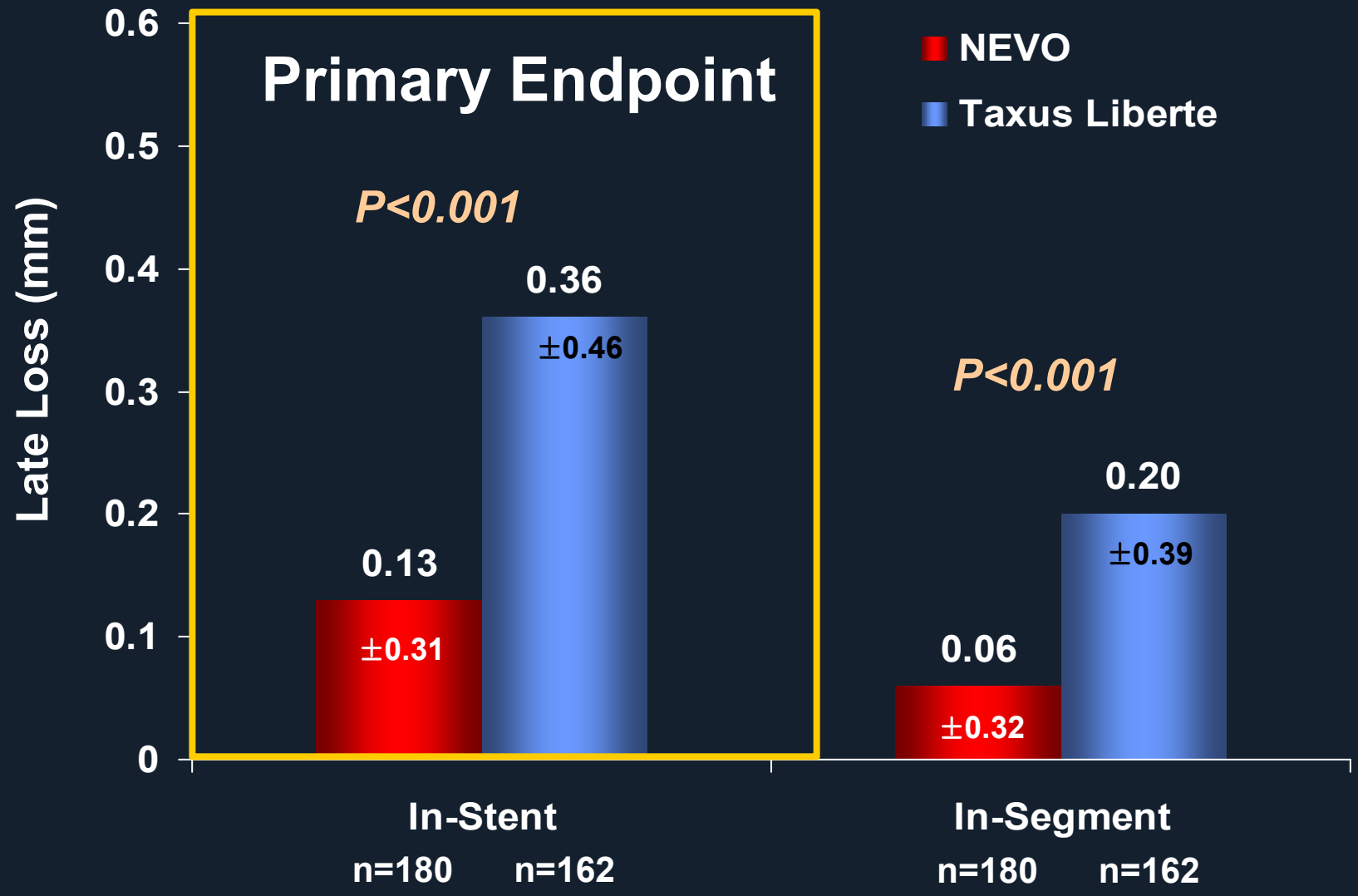
Polymer Structure and Degradation

8 days | 30 days | 60 days | 90 days

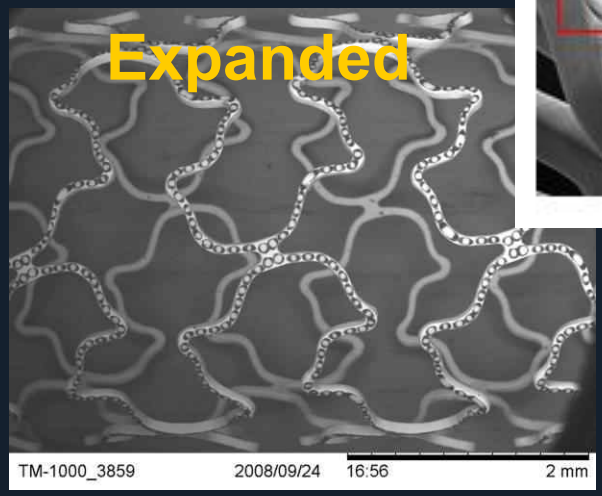


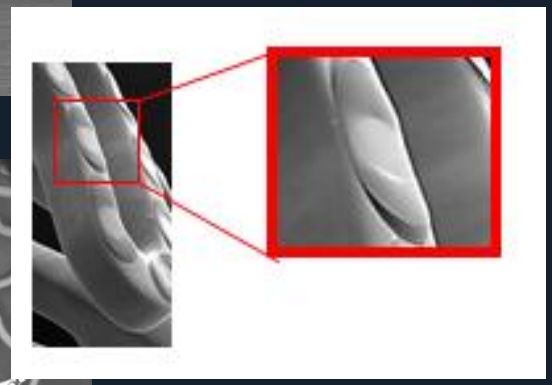
- **PLGA polymer resorbs within 3-4 months**
- **Begins 75% BMS and becomes 100% BMS within 3-4 mos**

Late Lumen Loss at 6-Months (N=342/394)



Properties of the JACTAX Stent





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 lmw biodegradable polymer decreases persistence time

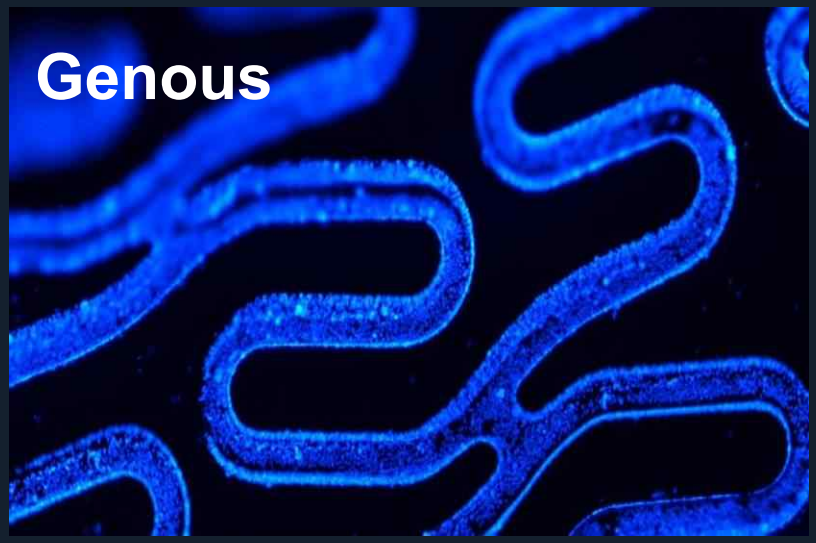
Stent platform

- Liberté ™pre-mounted stent (Boston Scientific)

Directional Sirolimus Biodegradable Abluminal Coating and Anti-CD34 Surface Modification

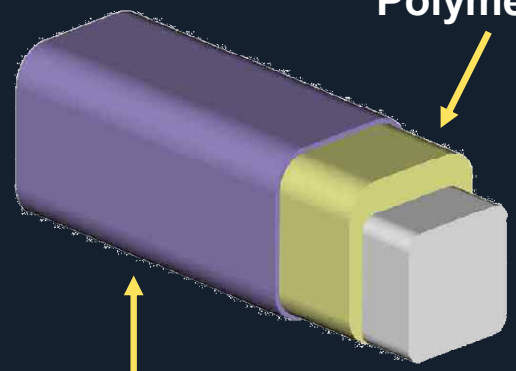
Genous Technology:

- Anti-CD34 surface to promote healing through rapid stent endothelialization



Genous-DES Technology:

- Rapamycin (5 µg/mm) applied in biodegradable SynBiosys polymer on the abluminal side



Future DES

New Drug Carrier Systems…2

- **Polymer-free Drug Delivery**
  - **Benefit – "essentially" BMS after drug delivery (maximal safety)**
  - **Issues – difficulties in prolonging drug elution**
  - **Examples: Translumina (Yukon), Biosensors (BioFreedom), MIV (Vestasync), Medtronic (drug-filled wire stent)**

Translumina: Unique Microporous Stent Surface

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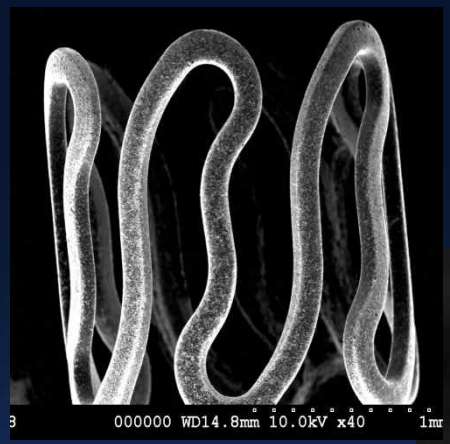
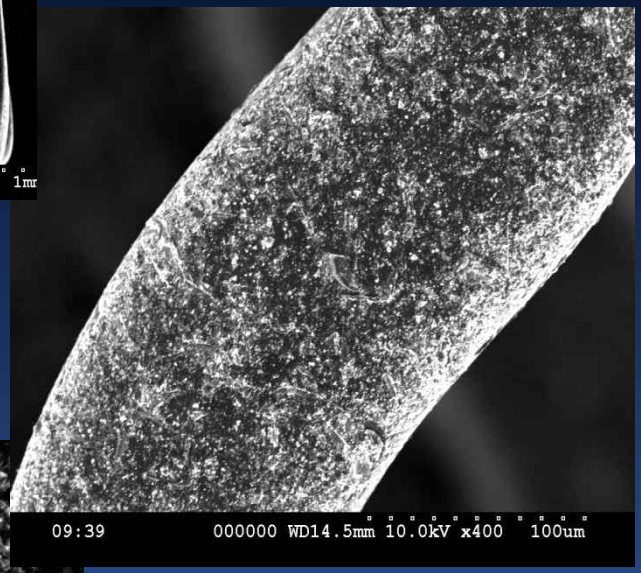
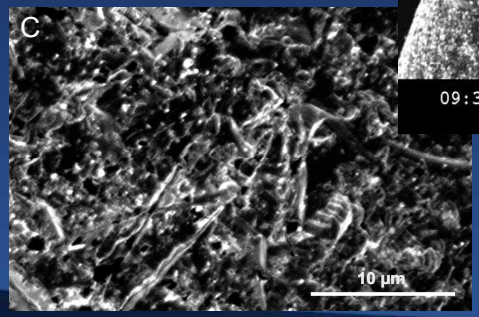
Stent Surface

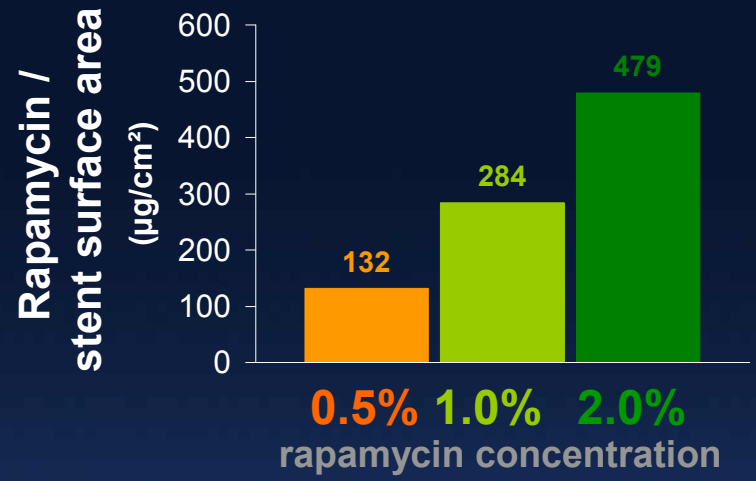




Yukon stent



Coating Capacity



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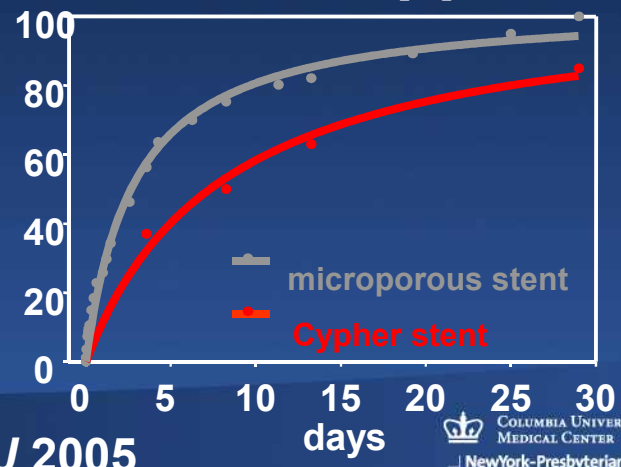

J Hausleiter et al. *Eur Heart J* 2005

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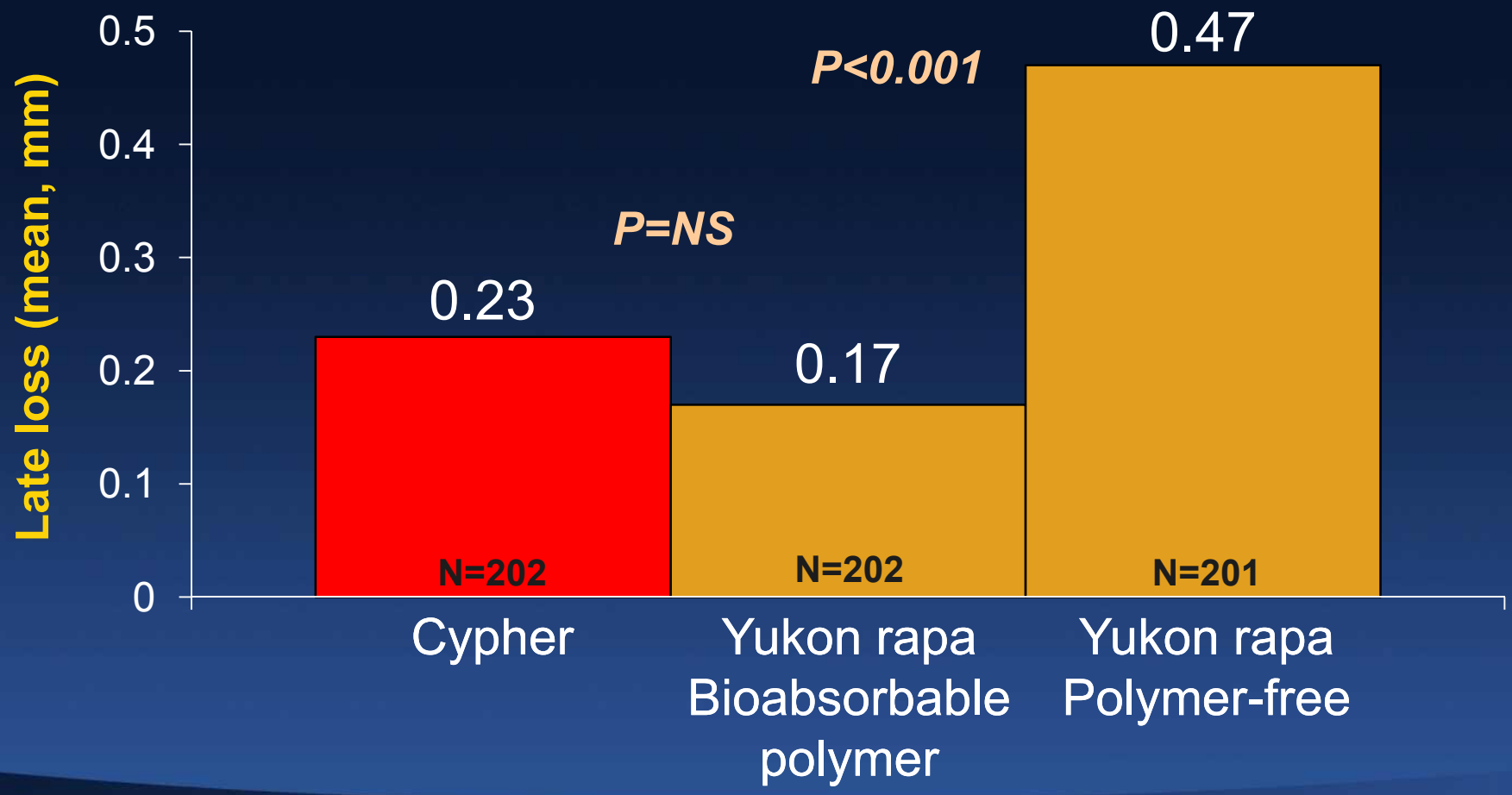
ISAR-STENT 3

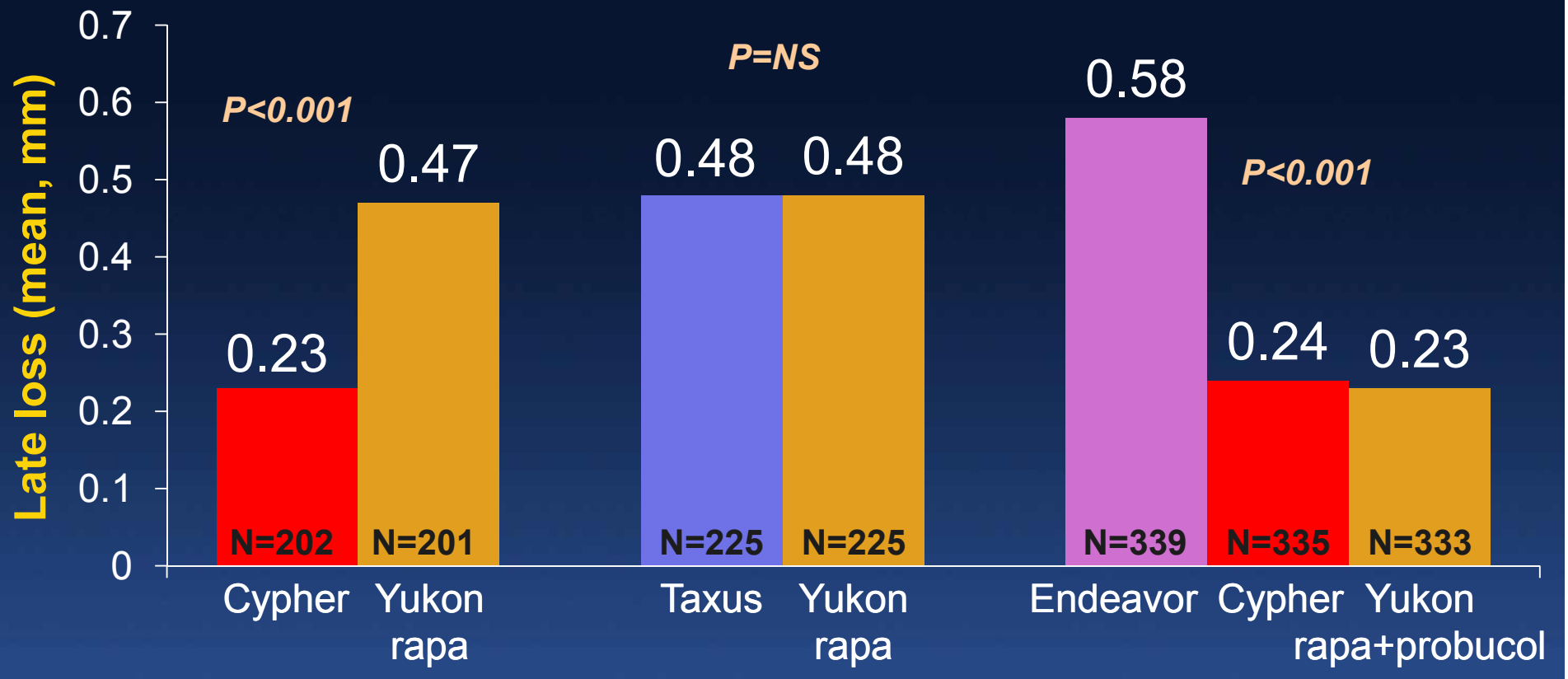
Bioabsorbable polymer vs. polymer-free

- In-stent late loss at 6-8 months-



Mehilli J et al. Eur Heart J 2008

Rapamycin-eluting Yukon Stent
Polymer-free
- In-stent late loss at 6-8 months-



ISAR-TEST 3 | **ISAR-TEST 1** | **ISAR-TEST 2**

Mehilli J et al.
Eur Heart J 2008

Mehilli J et al.
Circulation 2006

Byrne RA et al.
JACC 2010

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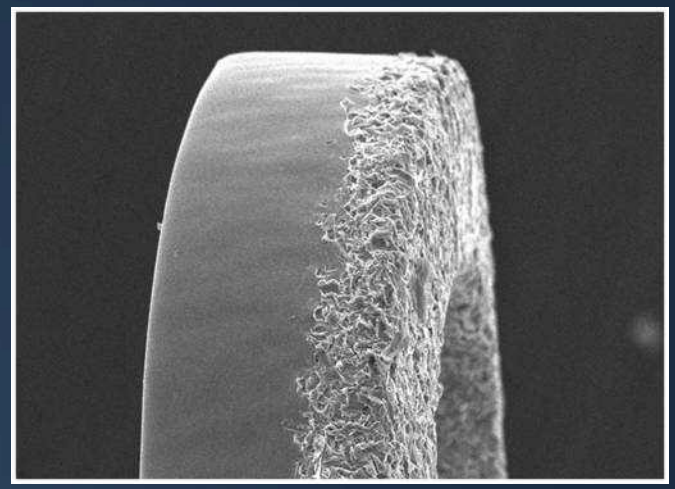
BioFreedom Stent (Biosensors)

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

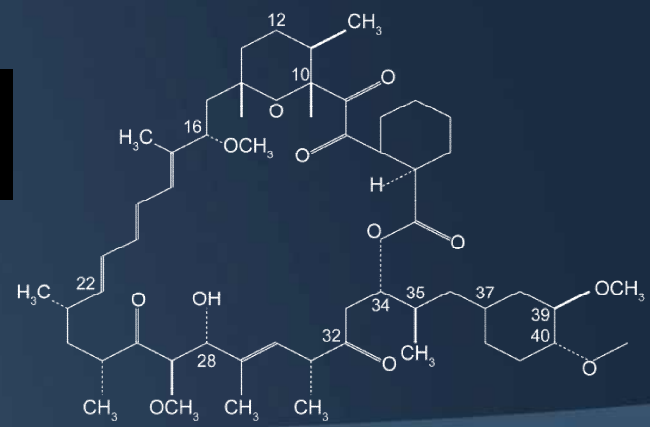
Potential advantages

- 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



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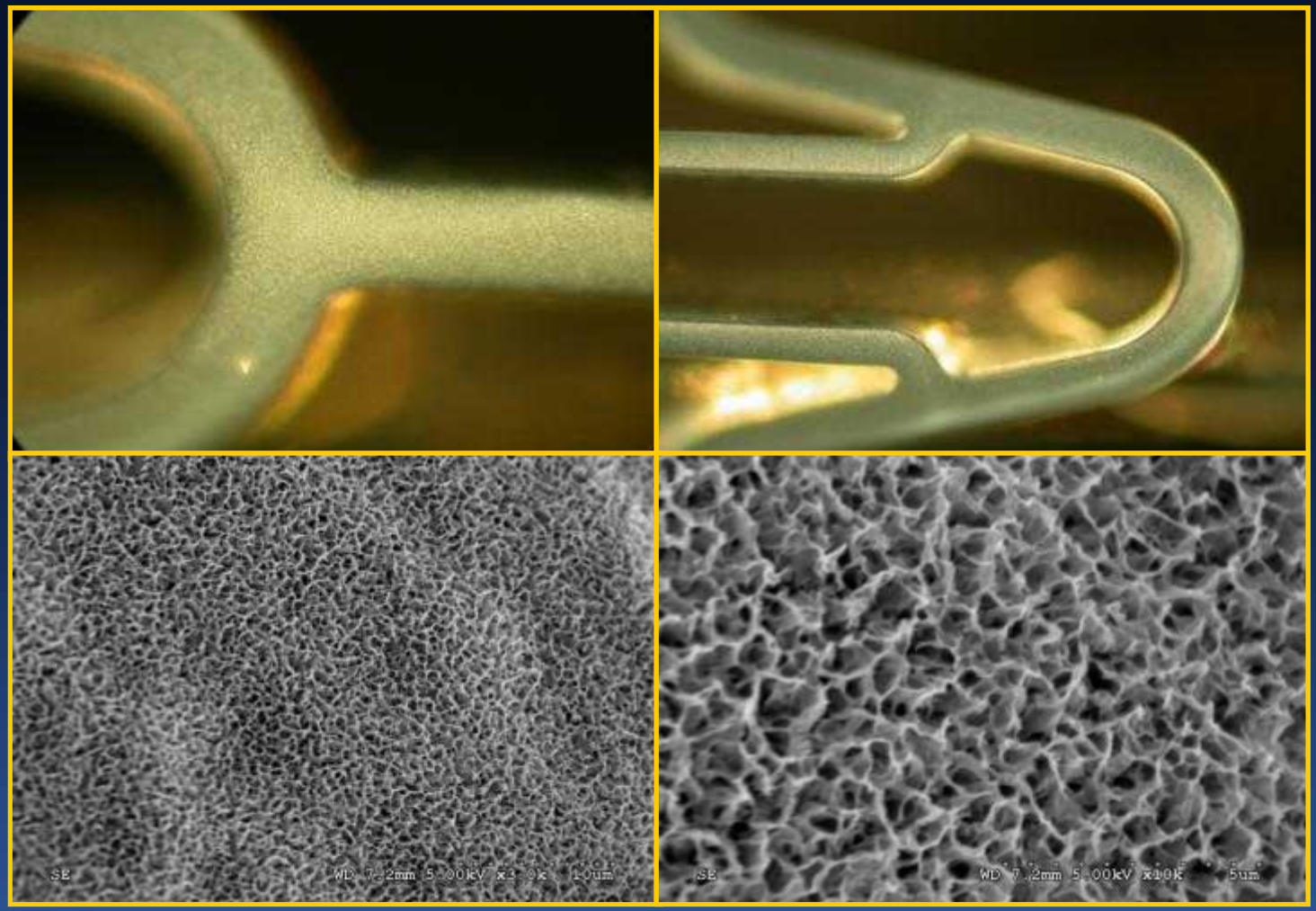
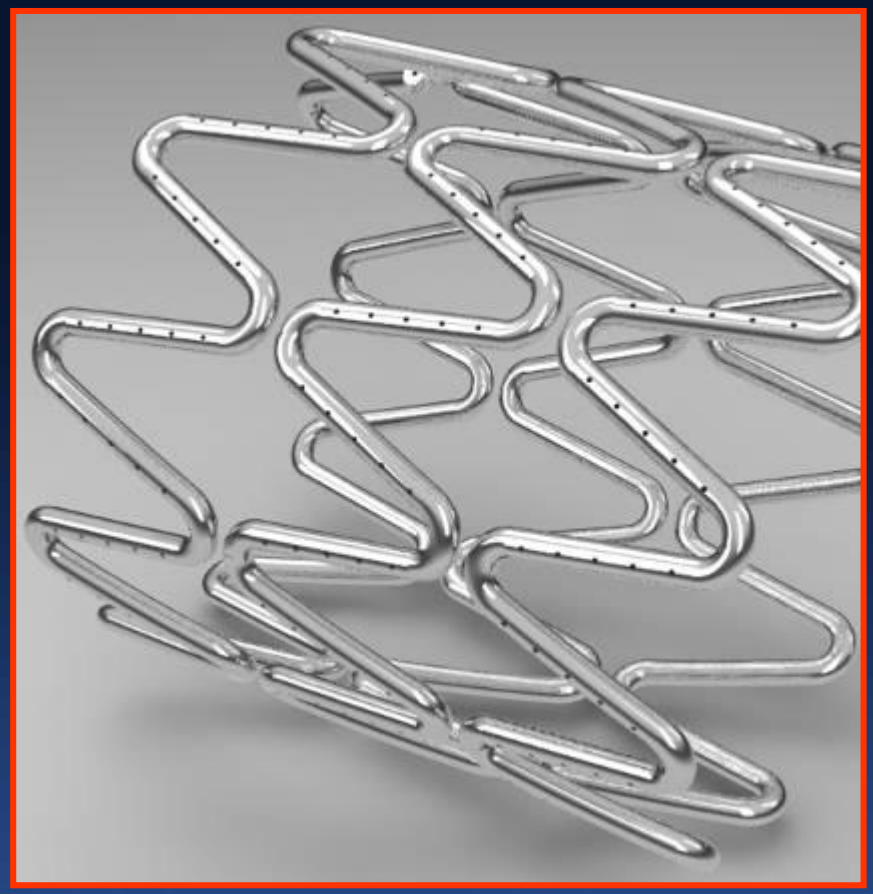
MIV: 3D MicroPorous Nanofilm Hap

Polymer-free DES (Vestasync)

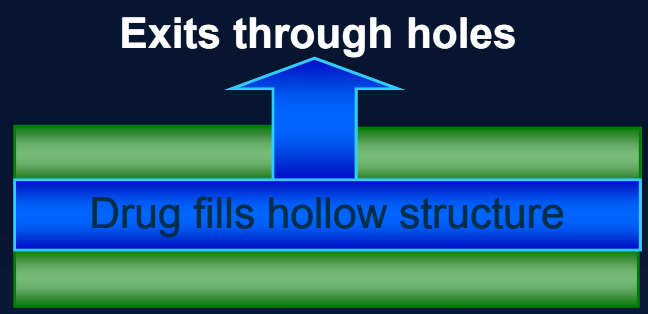


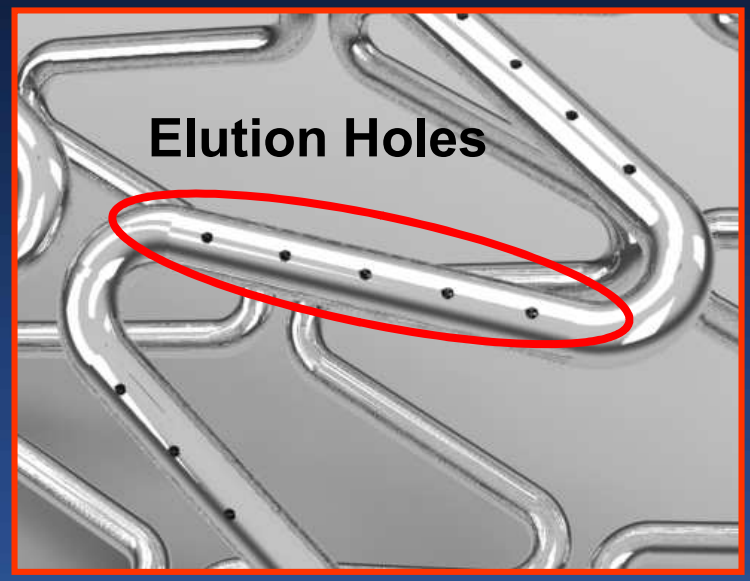
Drug Filled Stent (Medtronic)

Drug elution controlled by diffusion physics



No Polymer!





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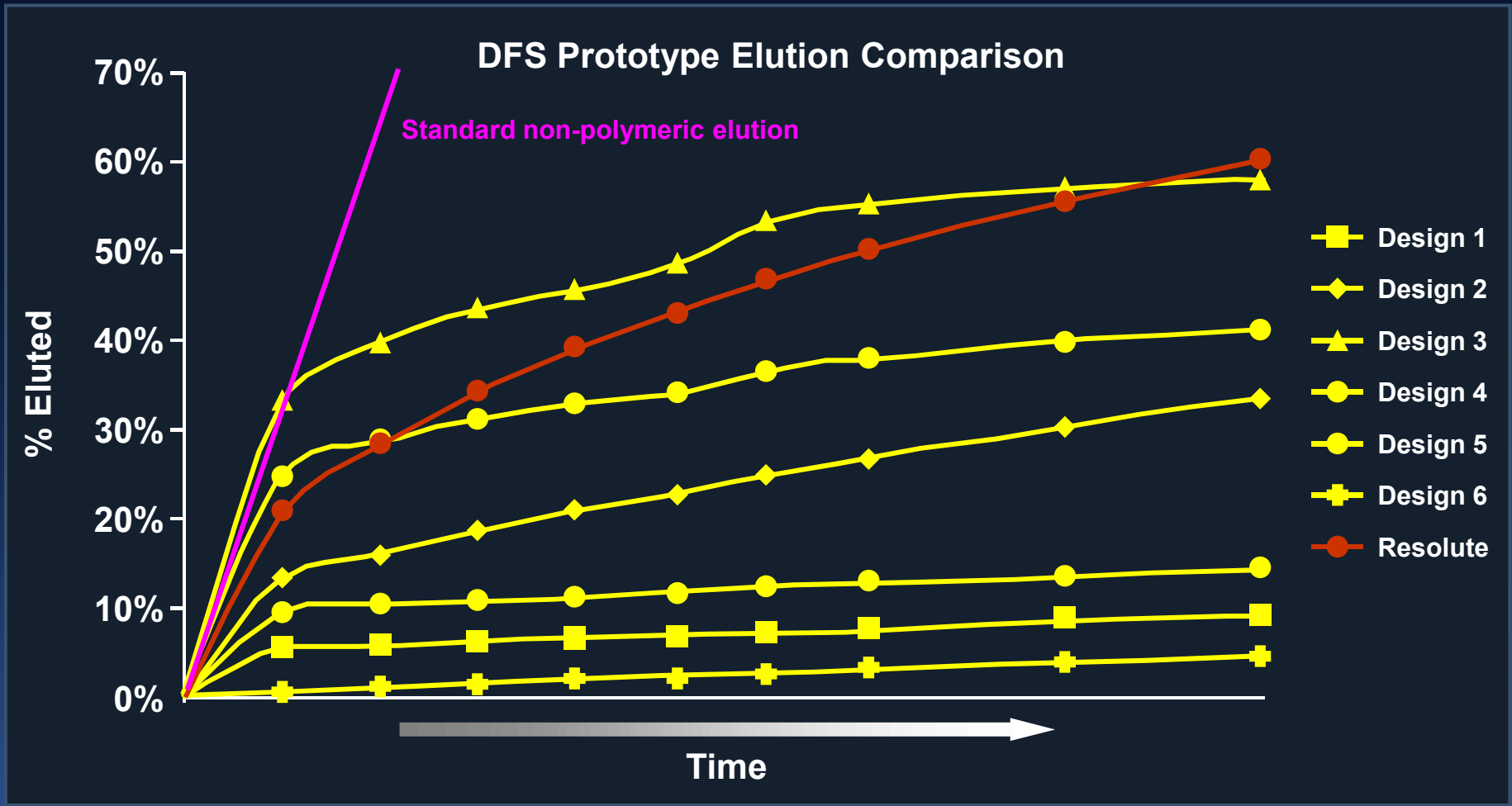

Preliminary testing suggests a variety of elution profiles possible.

Summary Conclusions

- Future DES are focusing on drug carrier enhancements to reduce safety concerns
  - *Bioabsorbable polymer-based drug delivery* – many versions, much promise, insufficient long-term clinical data to assess incremental value
  - *Polymer-free drug delivery* – best chance for "BMS-like" safety profile, BUT more difficult to achieve prolonged drug elution profiles, and little clinical data thus far
- Metallic stents with either bioabsorbable polymers or polymer-free systems will have to compete with the excellent safety and efficacy profiles of today's DES with nonerodable polymers, as well as with fully bioabsorbable stents and drug-eluting balloons