ENDEAVOR

ENDEAVOR
Clinical Trial Program

Raoul Bonan, MD

Components of the Endeavor Stent

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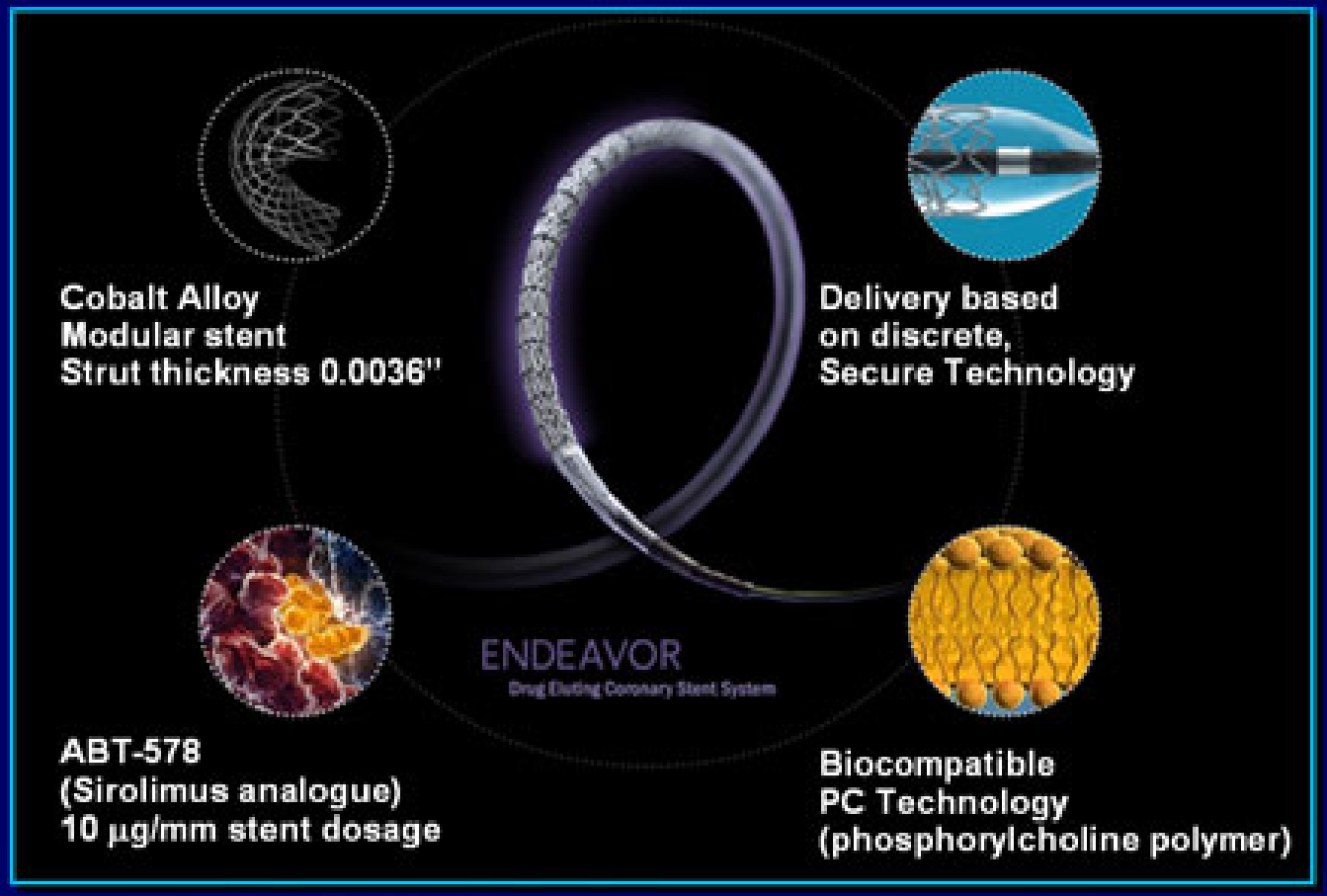


ENDEAVOR
Clinical Program Update

ENDEAVOR I	Phase I FIM 24 month results
ENDEAVOR II	Double-blind Randomized Trial 12 month results
ENDEAVOR II Registry	Open Label Safety Registry 8/9 month results
ENDEAVOR III	Confirmatory Trial vs. Cypher 12 month results
ENDEAVOR IV	Confirmatory Trial vs. Taxus
E-Five Registry*	Real-World Performance and Safety Evaluation

All ENDEAVOR trials analyzed in the same core lab.
* Post approval study

ENDEAVOR I

Phase I Trial "First In Man"

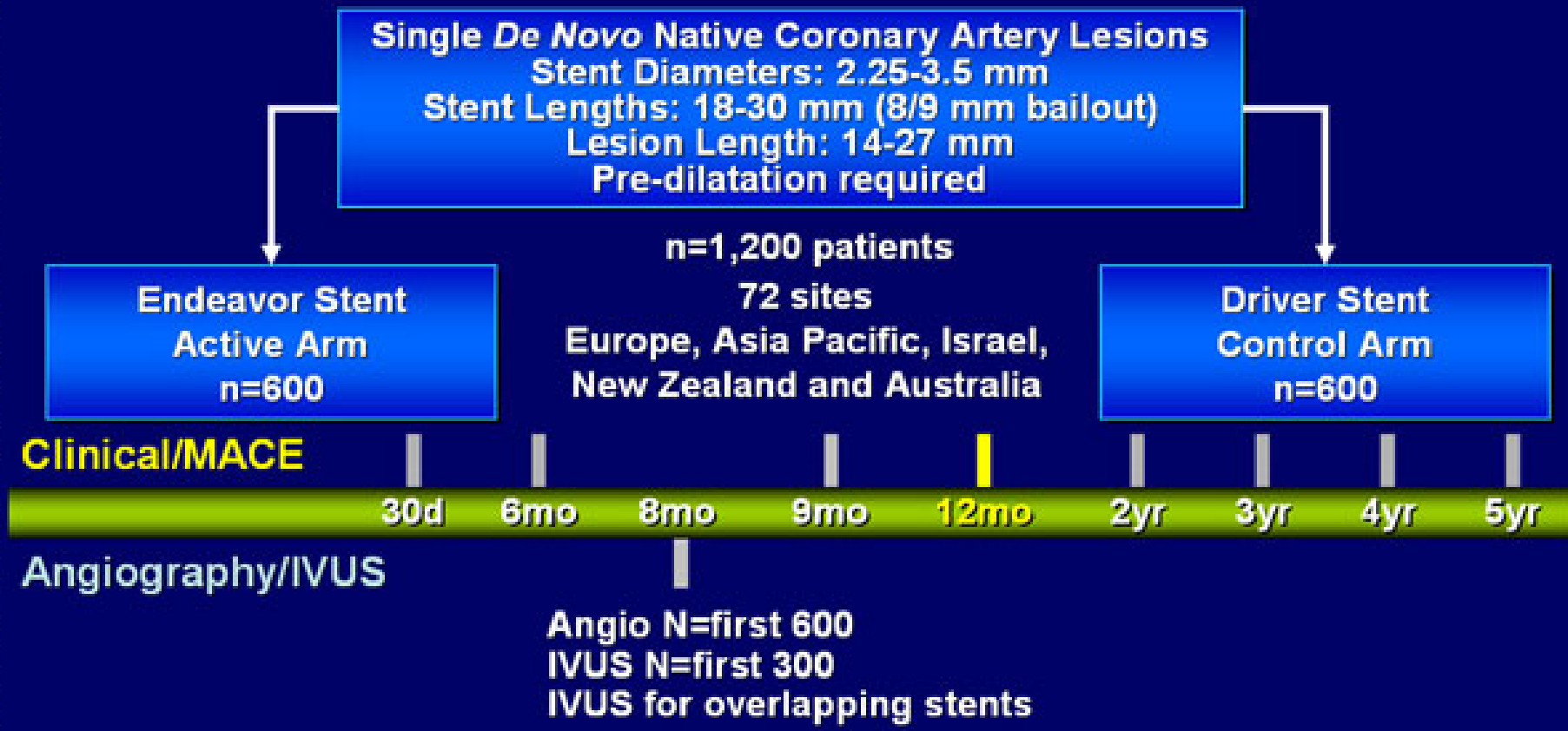
Single *De Novo* Native
Coronary Artery Lesions (Type A-C)
Stent Diameter: 3.0-3.5 mm
Stent Length: 18 mm
Lesion Length: <15 mm
Pre-dilatation required

n=100 patients
8 sites
Australia and New Zealand

Primary Endpoints: MACE at 30 days and late loss (QCA) at 4 months
Secondary Endpoints: TVF and TLR at 9 months, late loss at 12 months
Antiplatelet therapy for 3 months 10 µg ABT-578 per mm stent length

ENDEAVOR II

Randomized, Double-Blind Trial Design



Primary Endpoint: TVF (cardiac death, MI, TVR) at 9 months
Dual antiplatelet therapy for 3 months
10 μg ABT-578 per mm stent length

ENDEAVOR III

Multicenter Randomized Trial

3:1 Randomization

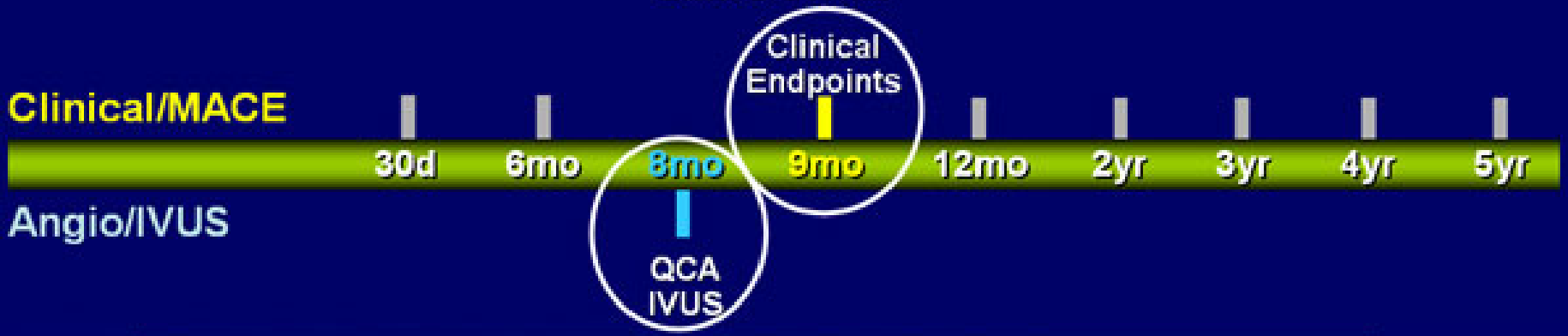
Single Blind – Single Vessel – No Staging

Single *De Novo* Native Coronary Lesion
Vessel Diameter: 2.5-3.5 mm
Lesion Length: 14-27 mm
Stent Lengths: 18–30 mm (8/9) mm bailout
Pre-dilatation required

Endeavor Stent
n=327

n=436 patients
30 sites
United States

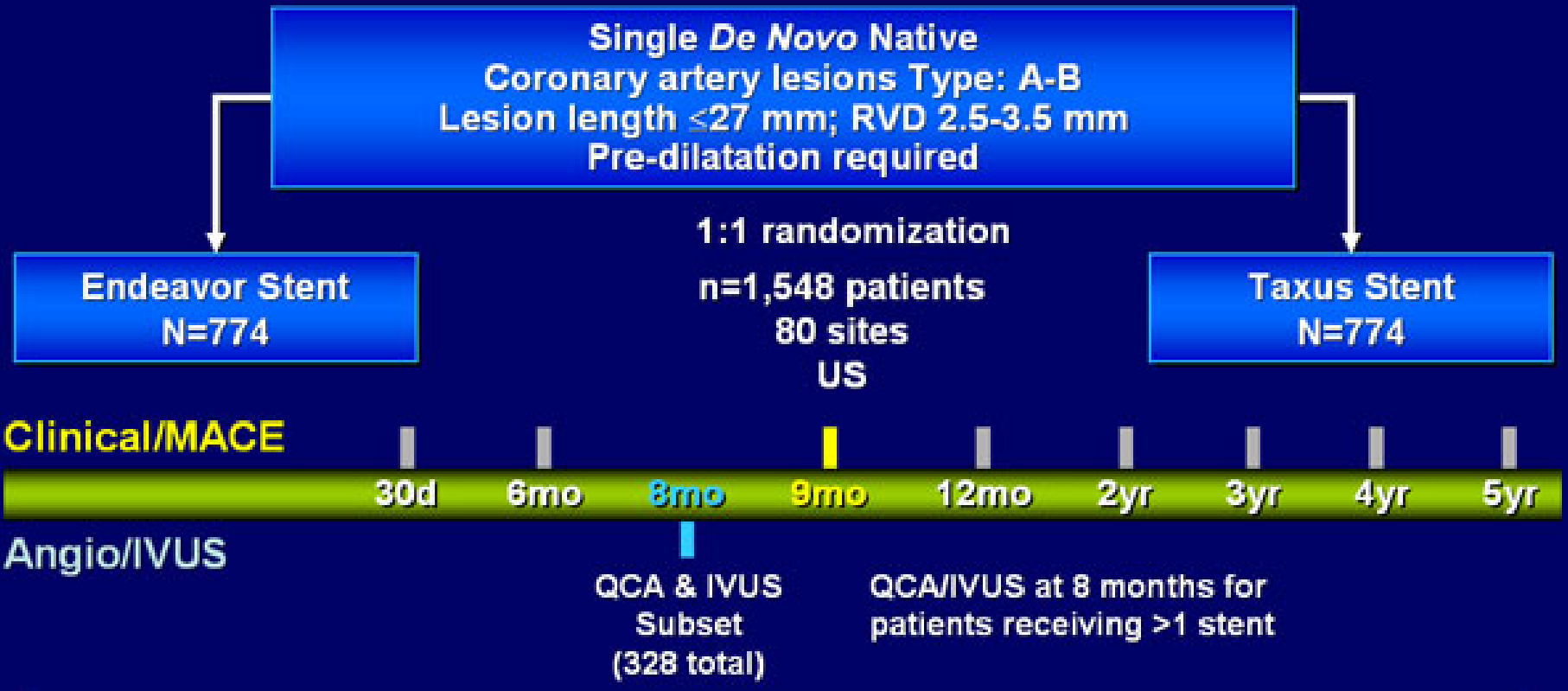
Control Cypher Stent
n=109



Primary Endpoint: In-segment late lumen loss by QCA at 8 months
Secondary Endpoints: TLR, TVR, TVF at 9 months & ABR at 8 months
Antiplatelet therapy for ≥3 months 10 µg ABT-578 per mm stent length

ENDEAVOR IV

Randomized, Single-Blind, Multicenter Trial



Primary Endpoint: TVF at 9 mos
Secondary Endpoints: In-segment % DS at 8 mos; TSR and TVR at 9 mos; MACE 1, 6, 9, 12 mos
Antiplatelet therapy for ≥6 months
10 µg ABT-578 per mm stent length

E-Five

Prospective, Multicenter Registry Assessing Safety in a Real World Patient Population

Single and Multiple Coronary Artery Lesions
Stent Diameters: 2.25-4.0 mm
Stent Length: 8/9-30 mm

n=8,000 patients
200 sites
Europe, Asia Pacific, Israel, New Zealand, South America

Primary Endpoint: MACE at 12 months

Secondary Endpoints: MACE at 30 days and 6 mo, Stent thrombosis, procedural success rate; device success rate; lesion success rate

Antiplatelet therapy for ≥ 3 months

10 µg ABT-578 per mm stent length

*Limited number of centers and specific patient subset.

DES Use Considerations

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- Deliverability (user-friendly features)
- Efficacy
  - Biologic activity (suppression of in-stent intimal hyperplasia)
  - Physiologic obstruction (stenosis severity)
  - Clinical benefit (prevention of repeat revascularization events)
- Safety (= stent thrombosis)

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Increasing Complexity Across Trials

Baseline Angiography	EI n=100	EII n=598	EII CA n=296	EIII n=323	Combined N=1317
Female Gender (%)	21.0	22.8	25.0	34.7	26.1
Diabetics (%)	16.0	18.0	25.8	29.7	22.5
B2/C lesions (%)	49	78.4	74.4	67.4	72.5
RVD (mm)	2.96	2.74	2.63	2.75	2.73
Lesion length (mm)	10.94	14.05	16.49	14.98	14.59
IIbIIIa (%)	10	13.2	7.1	44.0	19.1

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Confirms Endeavor Outstanding Deliverability

Study	ENDEAVOR Combined (N=1,307)
Procedure Success	97.1%
Lesion Success	99.7%
Device Success	99.2%

Device success defined as <50% residual in-segment percent diameter stenosis with assigned stent

Procedure success defined as <50% residual in-segment percent diameter stenosis with assigned stent and without in hospital MACE

- **Excellent procedural, lesion, device success in more than 1,300 patients**

Patent Lumen

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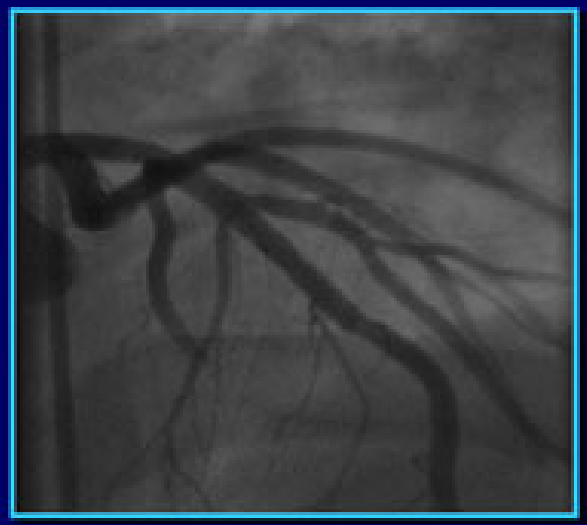
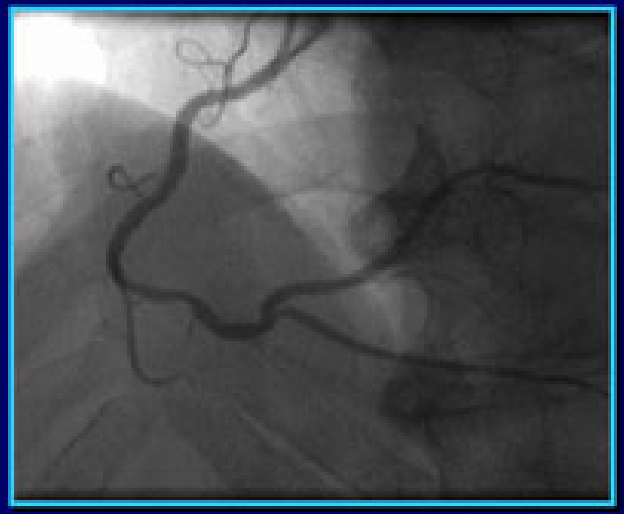
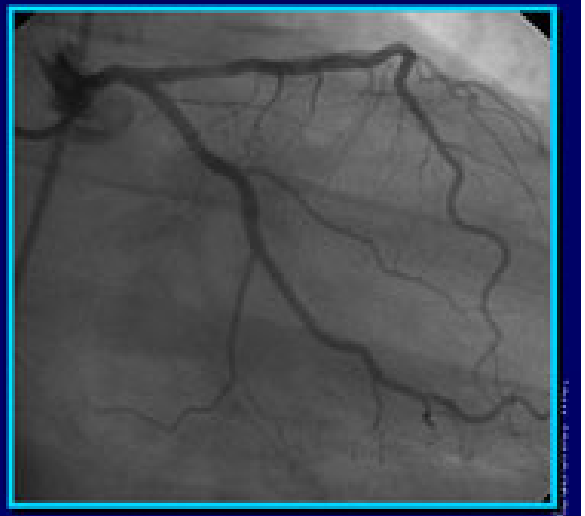
Indicative of Clinical Efficacy







Late loss	0.2 mm	0.4 mm	0.6 mm
RVD	3.59 mm	2.97 mm	2.70 mm

Patent lumen

Pivotal Trials: Late loss vs. TLR

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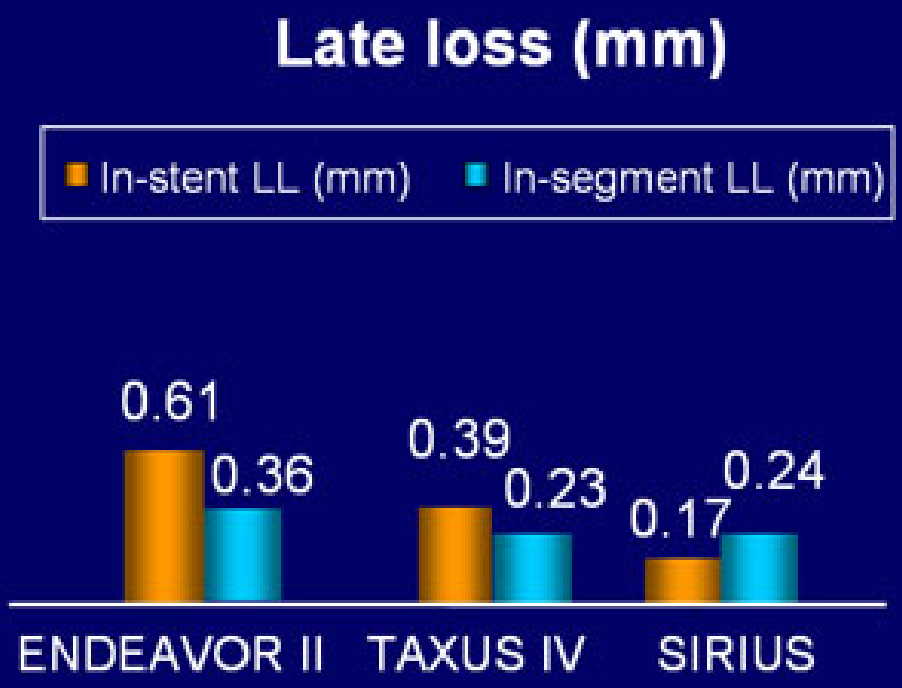
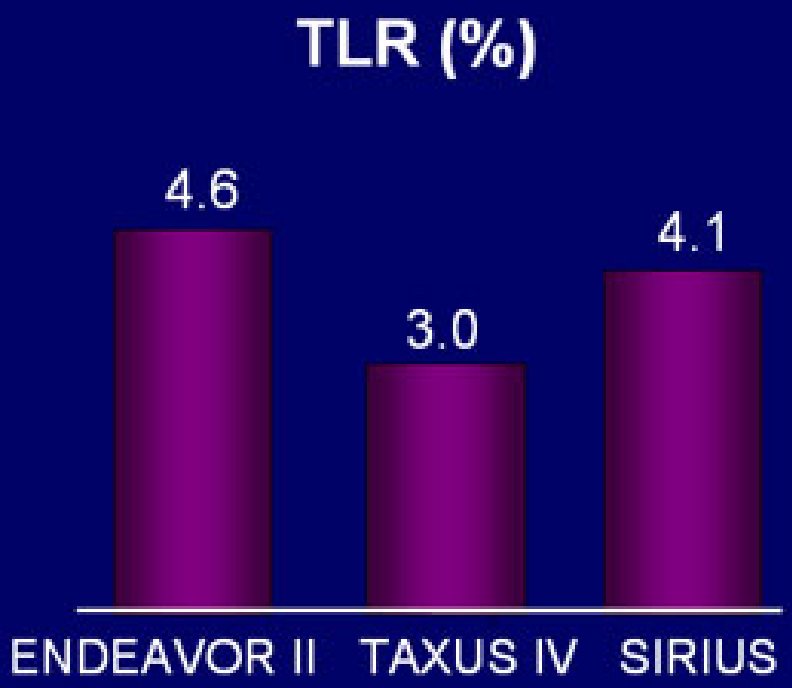
No Correlation between LL and TLR





Clinical results are not suitable for comparison

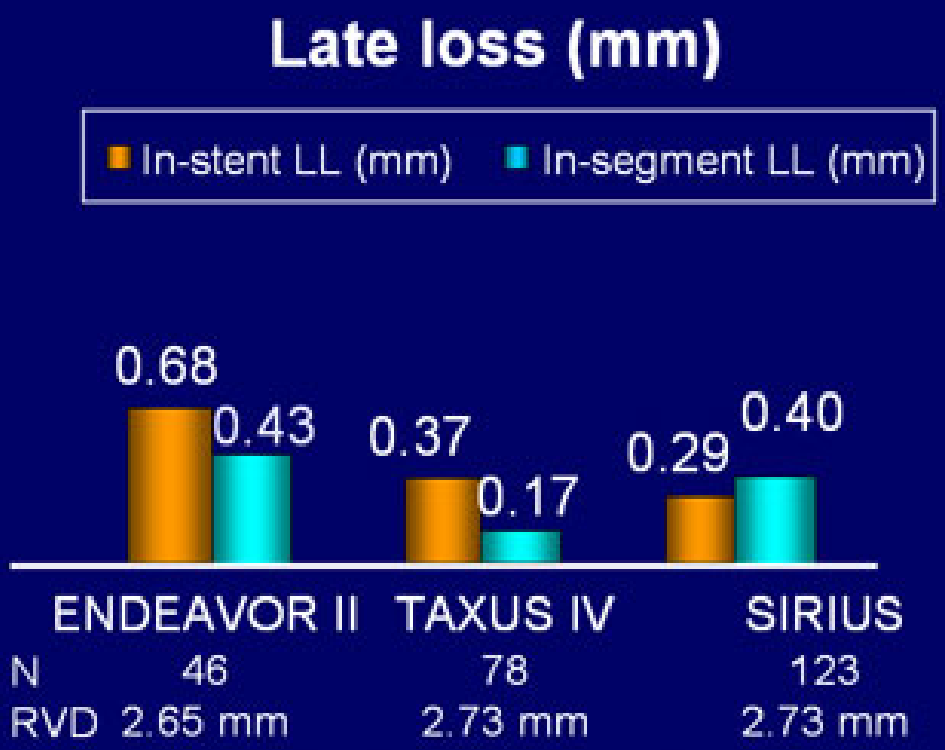
SIRIUS. Moses et al. NEJM 2003, 349, 1315-1323
TAXUS IV. Stone et al. NEJM 2004, 350, 221-231
SIRIUS diabetes subset. Circulation. 2004; 109: 2273-2278
TAXUS IV diabetes subset. J Am Coll Cardiol 2005; 45: 1172-9

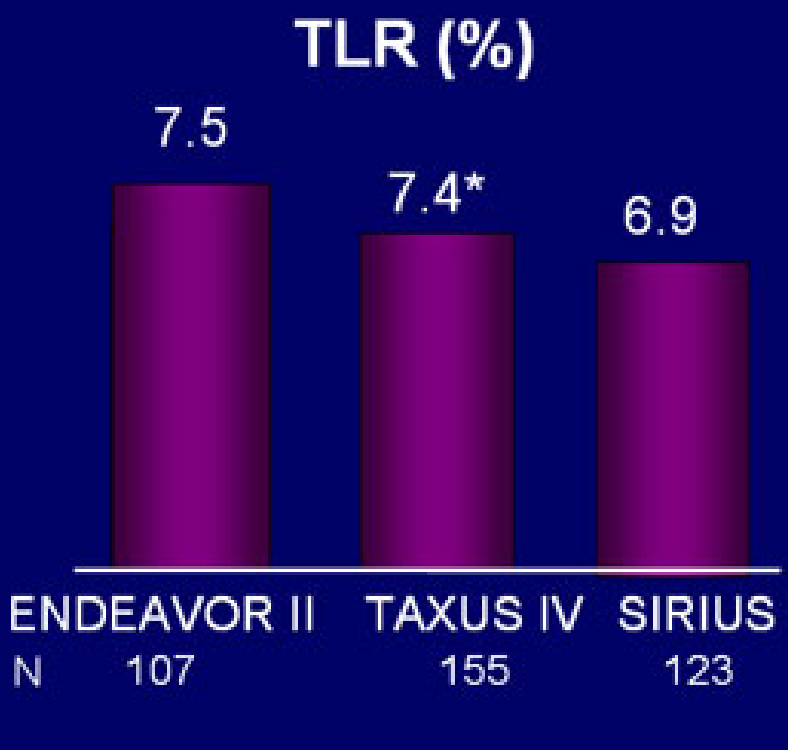
Pivotal Trials: Late loss vs. TLR

ENDEAVOR

No Correlation between LL and TLR

Diabetic Subgroups





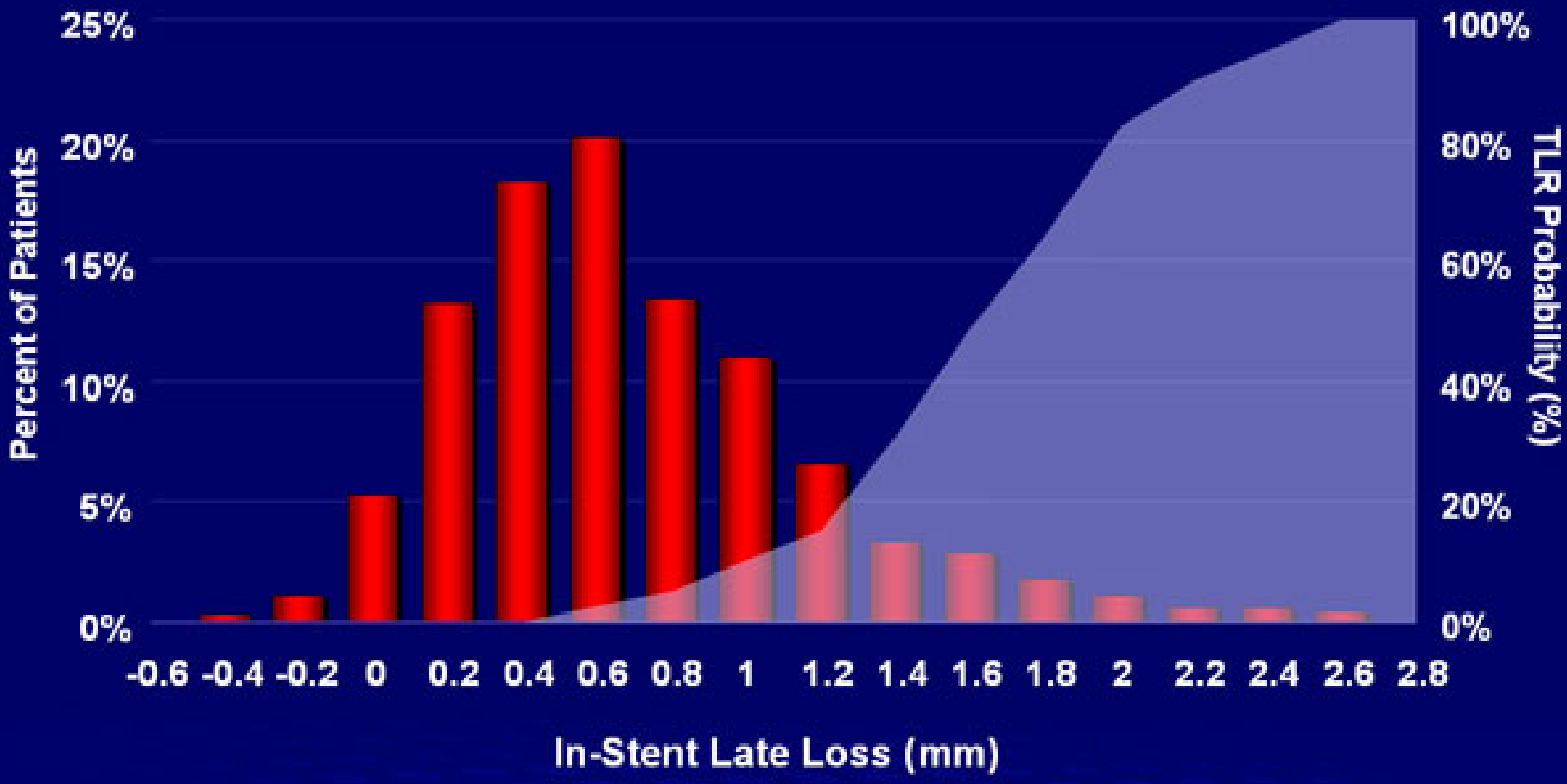
* 12 month analysis.

Clinical results are not suitable for comparison

SIRIUS. Moses et al. NEJM 2003, 349, 1315-1323
TAXUS IV. Stone et al. NEJM 2004, 350, 221-231
SIRIUS diabetes subset. Circulation. 2004; 109: 2273-2278
TAXUS IV diabetes subset. J Am Coll Cardiol 2005; 45: 1172-9

ENDEAVOR Trials: I-III

In-Stent LL/TLR Relationship (N=657)*



*Pts undergoing angiographic follow-up.

Consistent Clinical Results

TLR % Combined Studies EI, EII, EII CA and EIII

Study:	TLR % at 9 Months (n)
EI	**2.0% (2/100)**
EII	**4.6% (27/591)**
EII CA	**4.8% (14/289)**
EIII	**6.3% (20/316)**
Combined	**4.9% (63/1296)**

Clinical Events (%)

DES Arms From Randomized Trials

9 Month Results	EI n=100	EII n=591	EII CA n=289	EIII n=316	Combined N=1296
MACE (%)	2.0	7.3	10.4	7.6	7.6
TLR (%)	2.0	4.6	4.8	6.3	4.9
TVF (%)	2.0	8.0	13.1	12.0	9.6

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Clinical Events to 9 Months

	EI n=100	EII n=591	EII CA n=289	EIII n=316	Combined N=1296
MACE	2%	7.3%	10.4%	7.6%	7.6%
Death	0	1.2% [7]†	0.7%	0.6% [2]‡	0.8%
MI (all)	1%	2.7%	5.2%	0.6%	2.6%
Q-wave	0	0.3%	0.3%	0%	0.2%
Non Q-wave	1% [1]*	2.4%	4.8%	0.6%	2.4%
TLR	2%	4.6%	4.8%	6.3%	4.9%
TVR (non-TL)	0	1.5%	4.2%	6.0%	3.1%
TVF	2%	8.0%	13.1%	12.0%	9.6%

*Stent thrombosis at 10-days.
†2 of 7 deaths non-cardiac (1 lung cancer, 1 cerebral hemorrhage)
‡Non-cardiac deaths (lung cancer and cerebral hemorrhage)

Clinical Events (%)

DES Arms from Combined Trials

ENDEAVOR

Sources:
ENDEAVOR Pooled Clinical Events to 9 months, data on file at Medtronic, Inc.
TAXUS ACC 2005 Meta-Analysis (all patients), Greg Stone
CYPHER ACC 2005 Analyst Meeting

Clinical results are not suitable for comparison

Clinical Events (%)

DES Arms from Combined Trials

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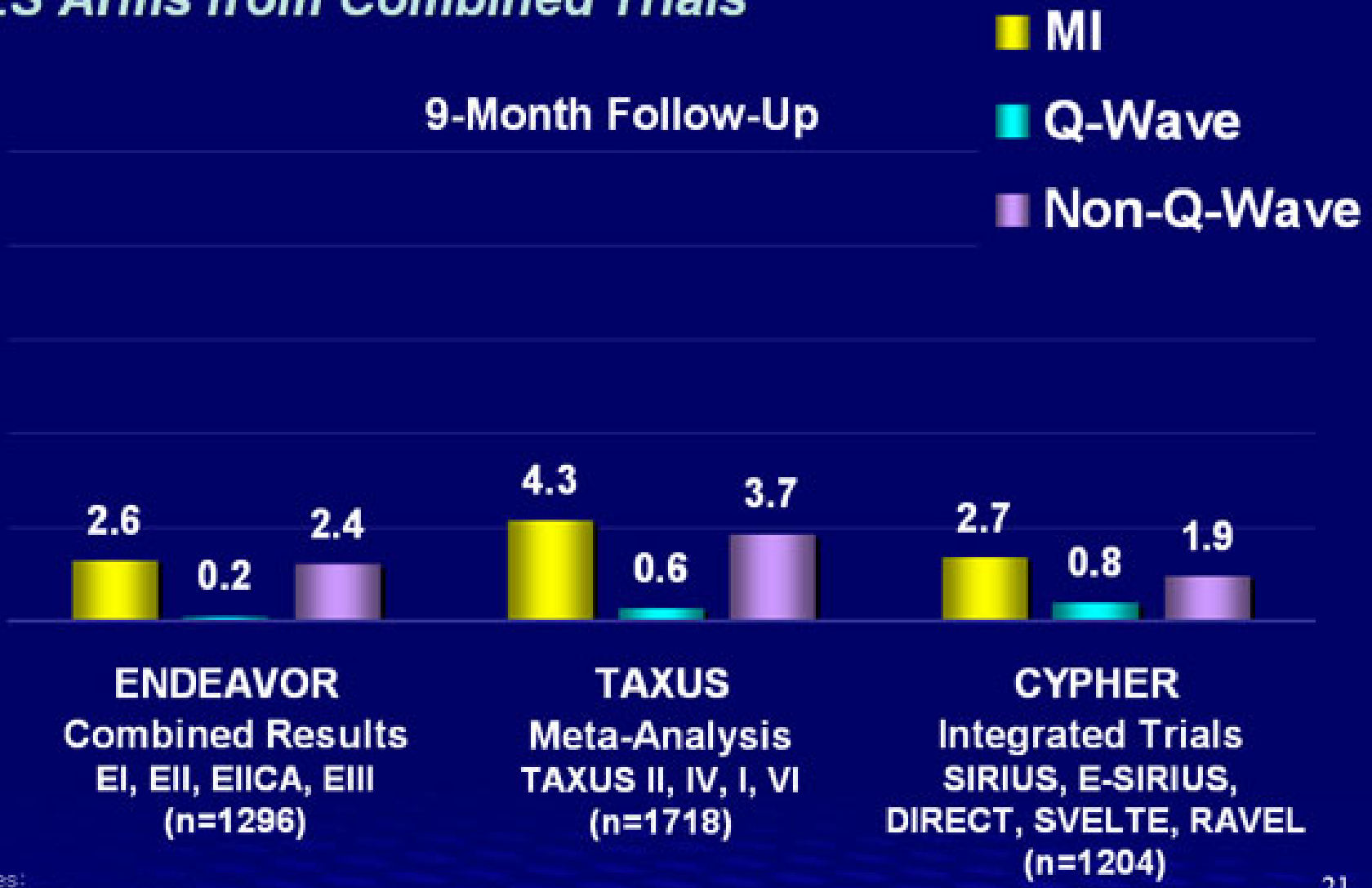

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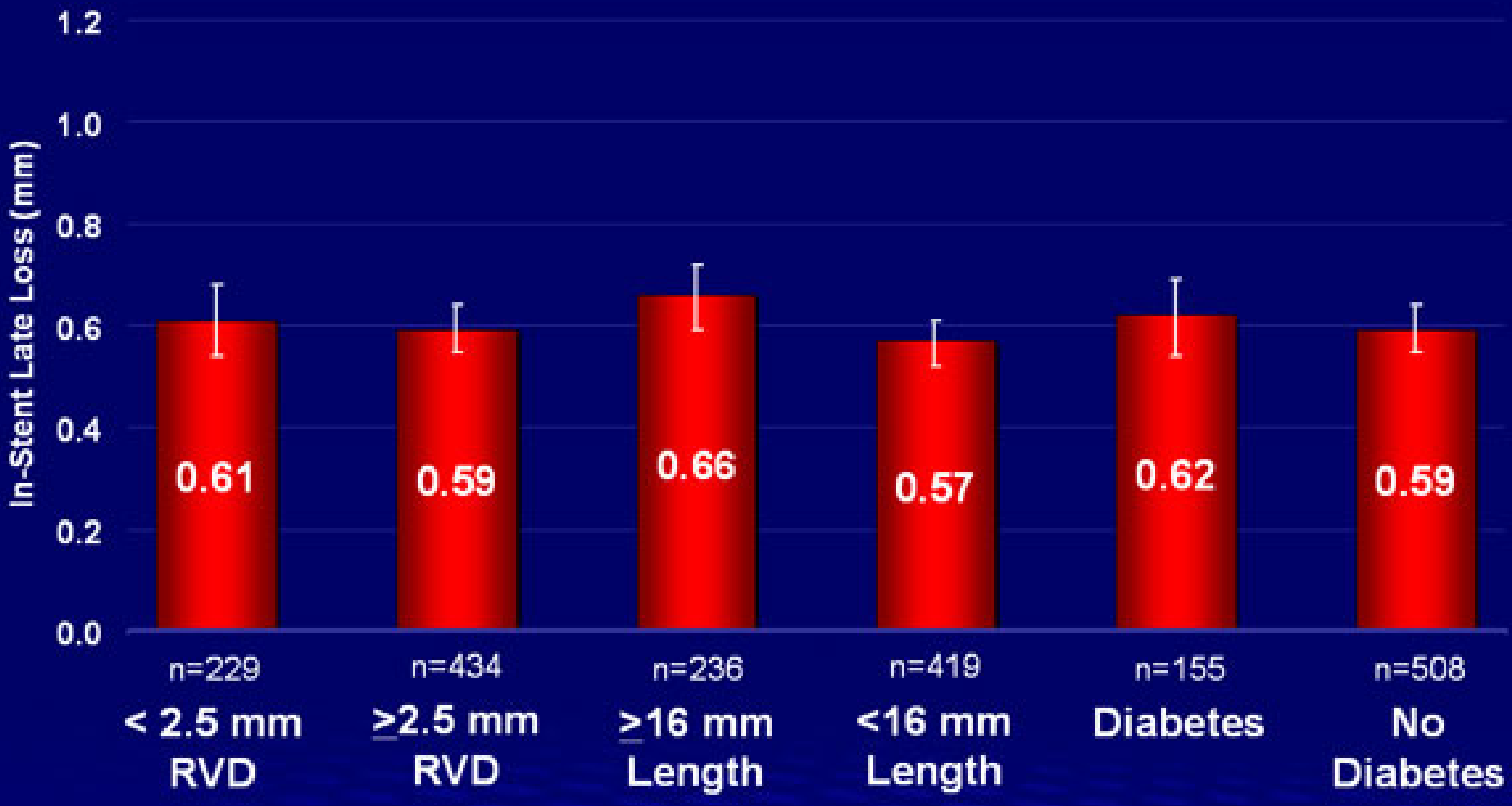
ENDEAVOR Clinical Program

No Difference in LL Across High Risk Subgroups



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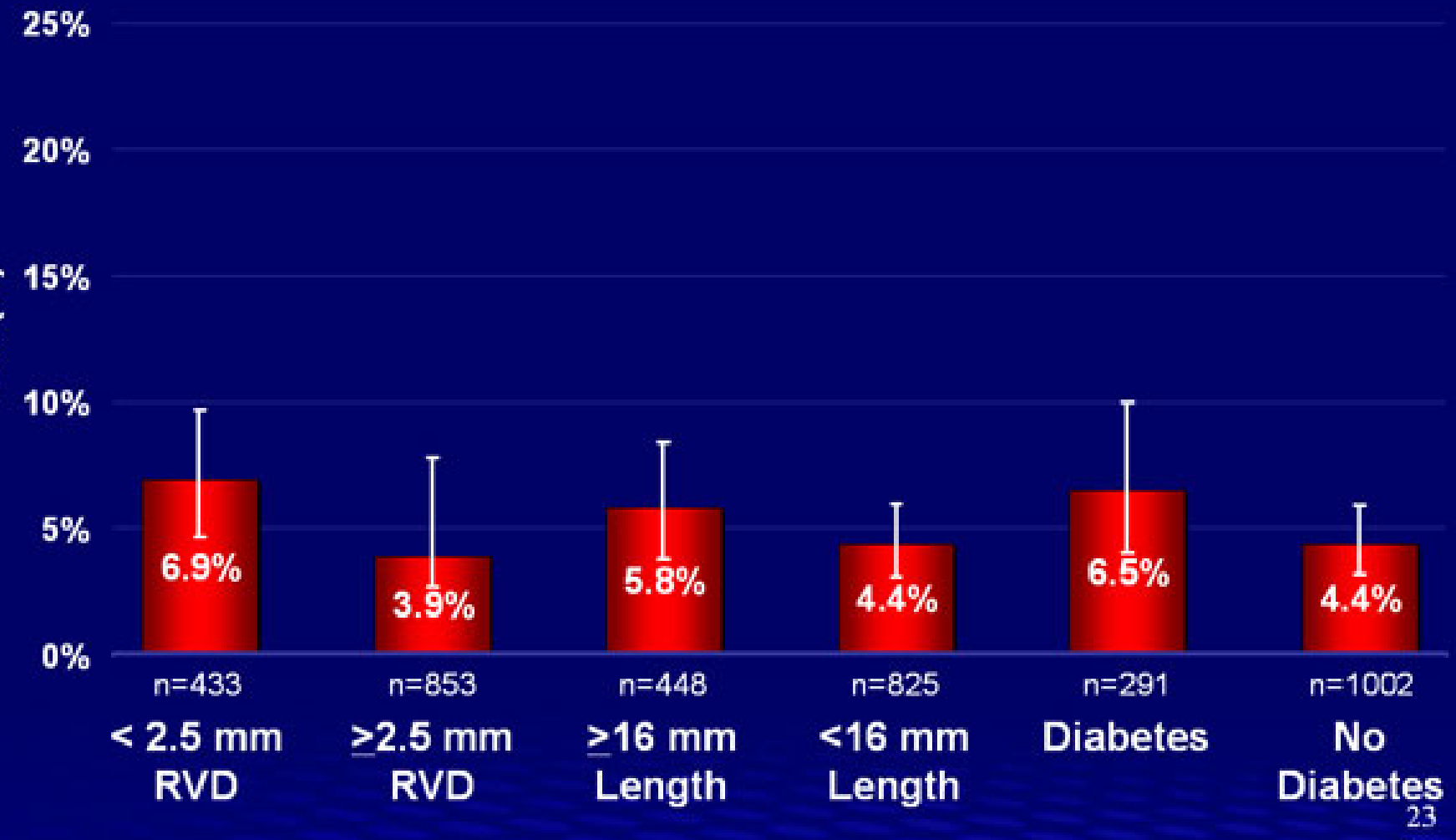
No Difference in TLR Rates Across High Risk Subgroups



Late Stent Thrombosis—Factors to Consider

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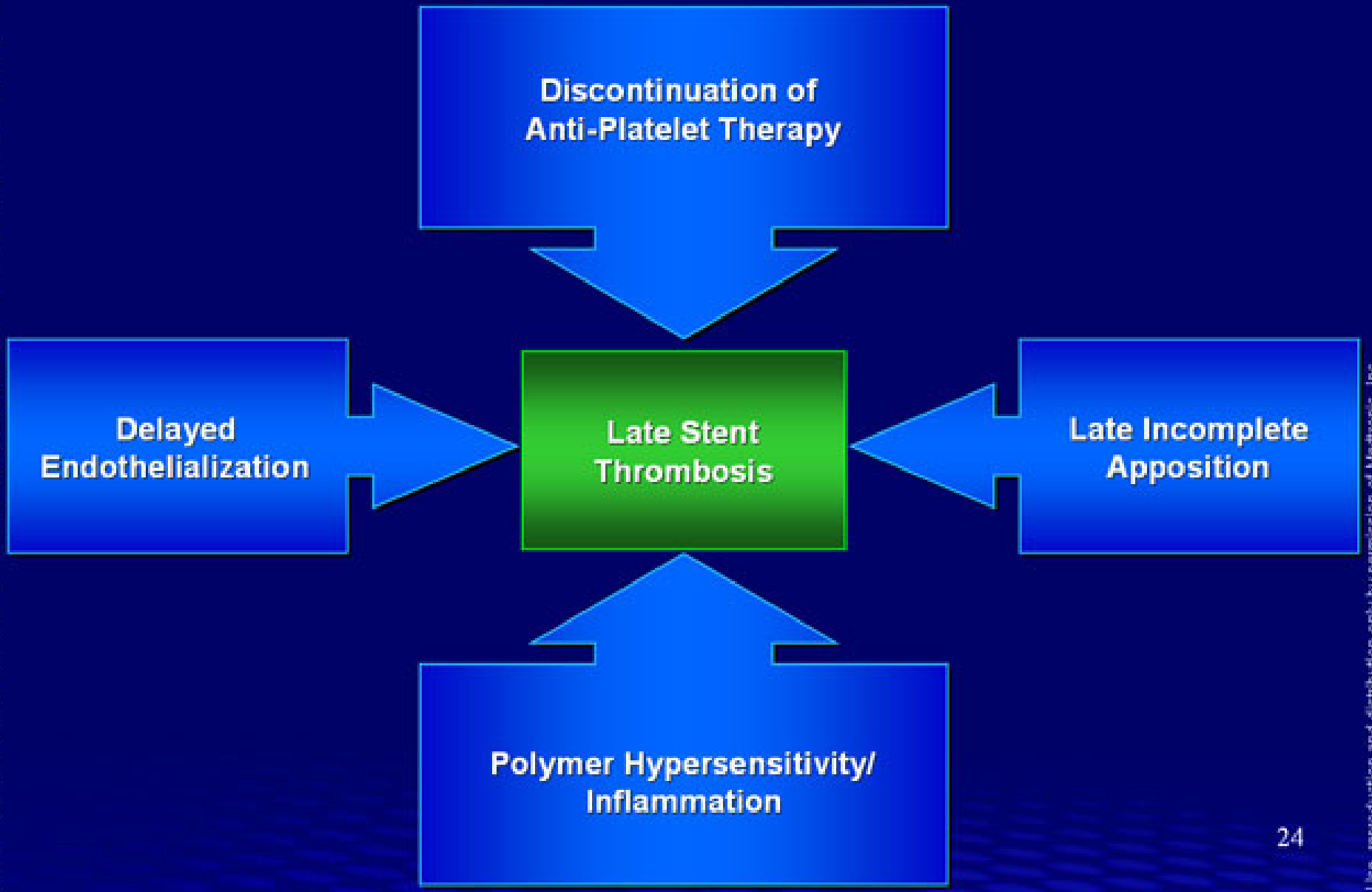

Late-Incomplete Apposition

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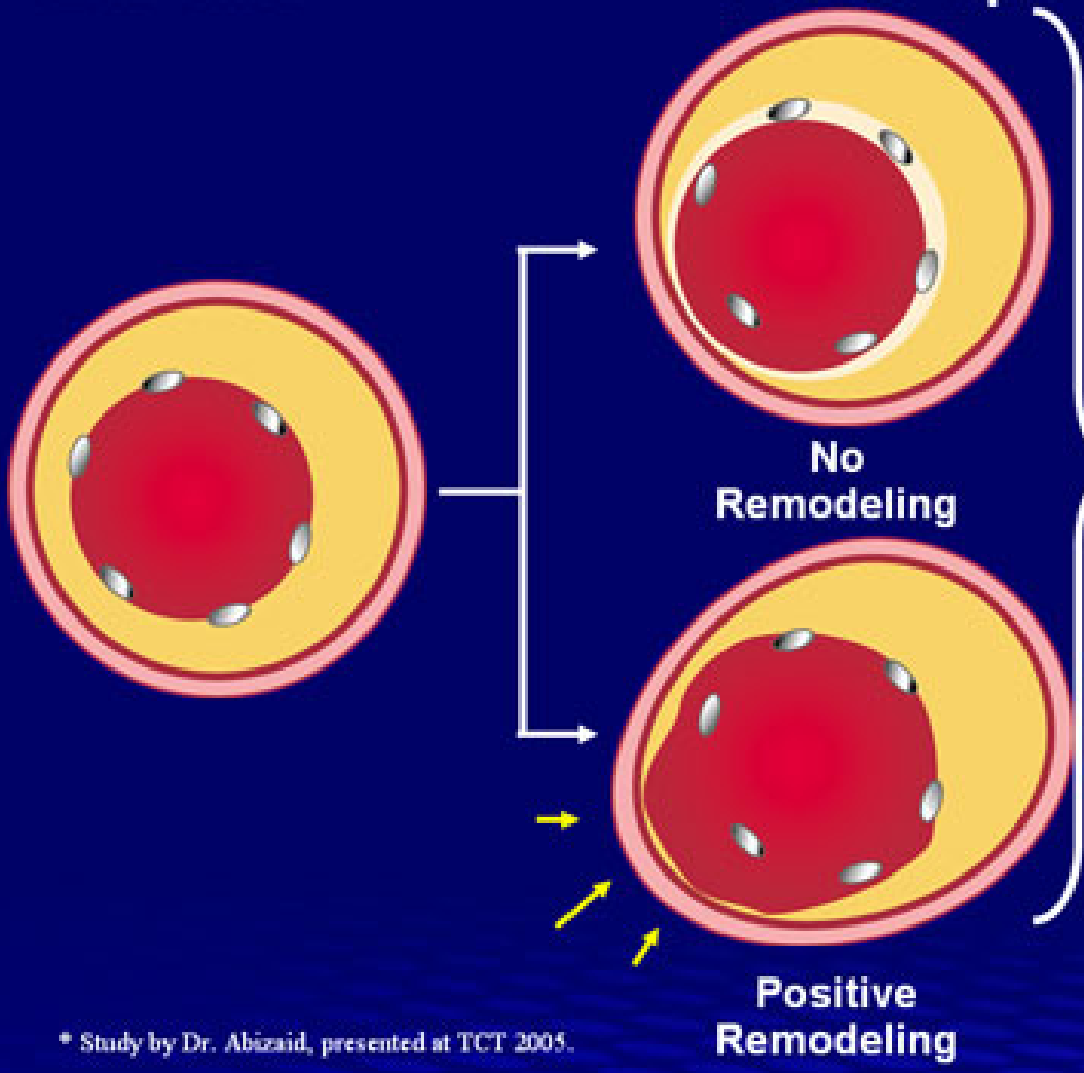
Potential for Stent Thrombosis



In a Taxus and Cypher study of patients with late incomplete apposition upon clopidogrel discontinuation:

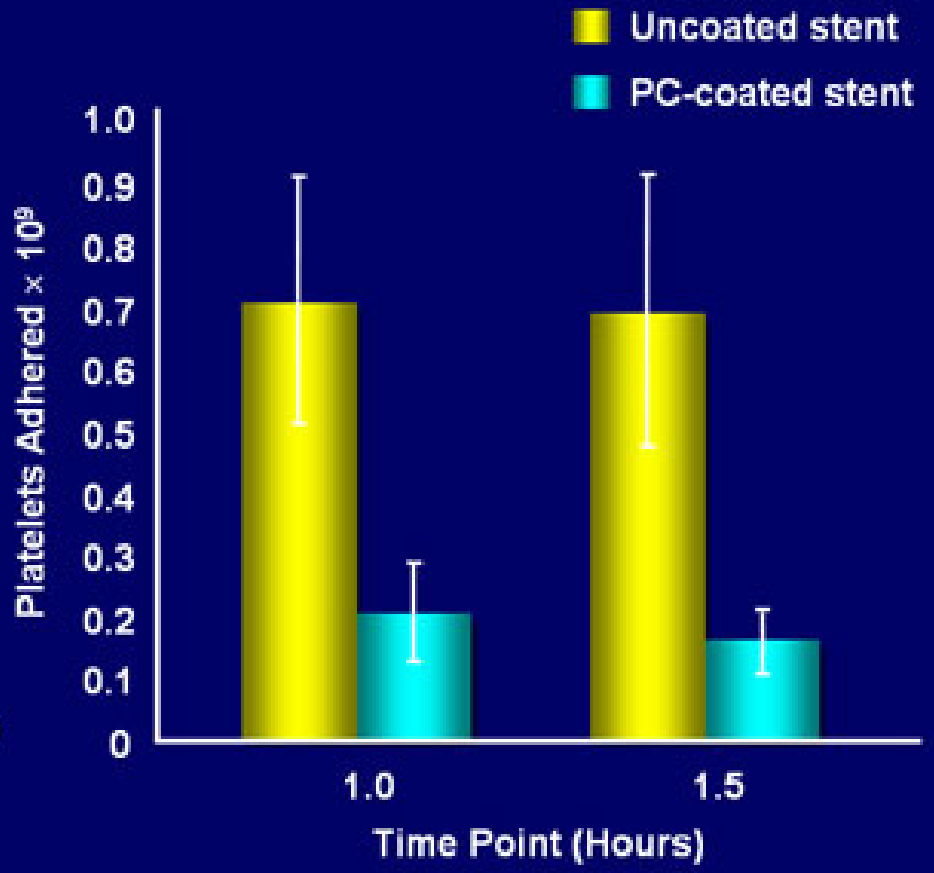
20% had stent thrombosis*

* Study by Dr. Abizaid, presented at TCT 2005.

PC Technology

Thrombo-Resistant

- Non-thrombogenic (hemocompatible)
  - Non-inflammatory
  - Hydrophilic: Inhibits protein adhesion
- PC coated stents showed less platelet adhesion compared to uncoated stents in a baboon-shunt flow model



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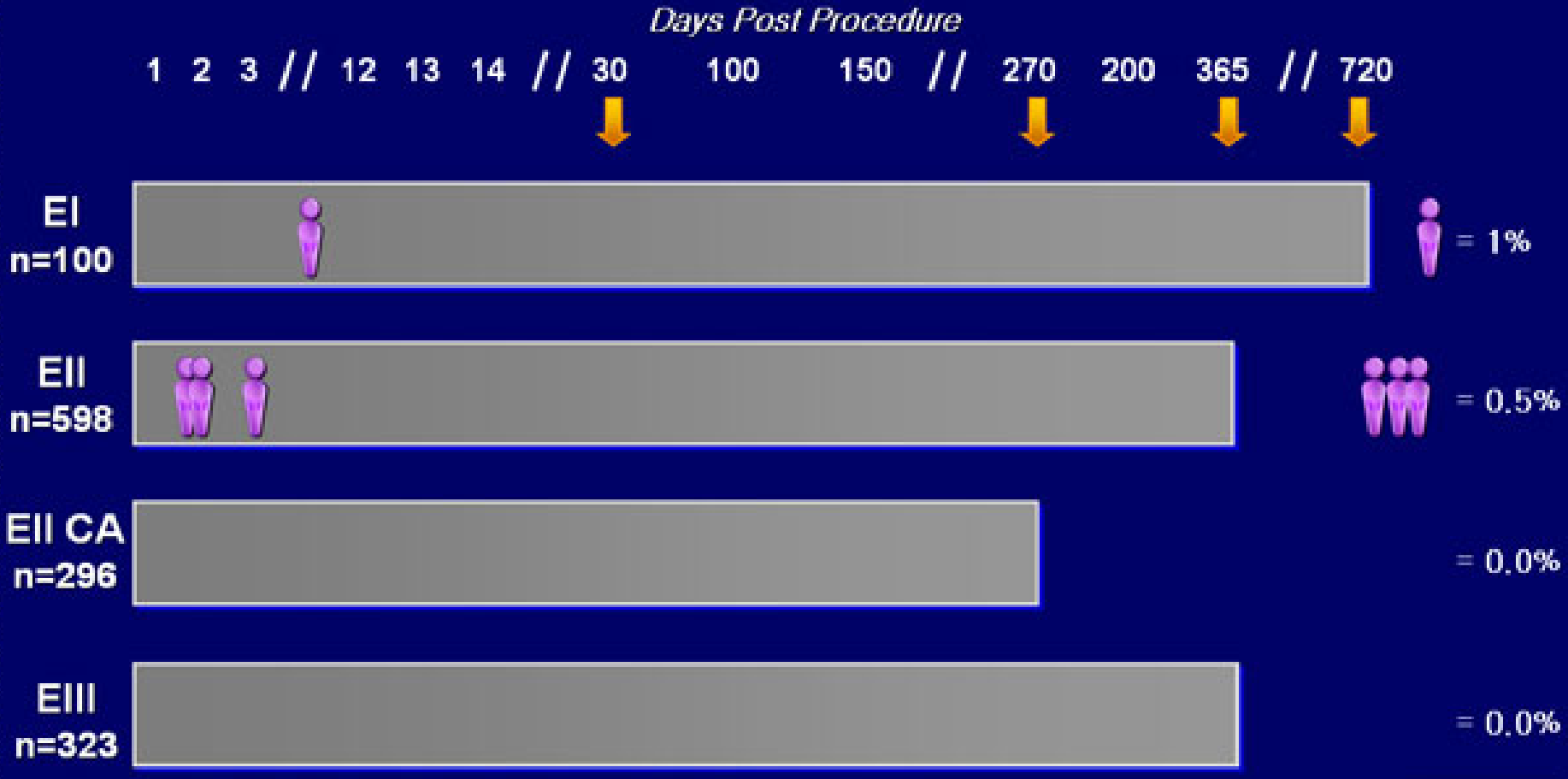
Safety Profile

No Late Stent Thrombosis in Over 1,300 Patients



Defined as angiographic thrombus or subacute closure within the stented vessel at the time of the clinically driven angiographic restudy for documented ischaemia (chest pain and ECG changes). Any death not attributed to a non-cardiac cause within the first 30 days is considered a surrogate for stent thrombosis in the absence of documented angiographic stent patency.

Overall Thrombosis = 0.3%
30

Safety:

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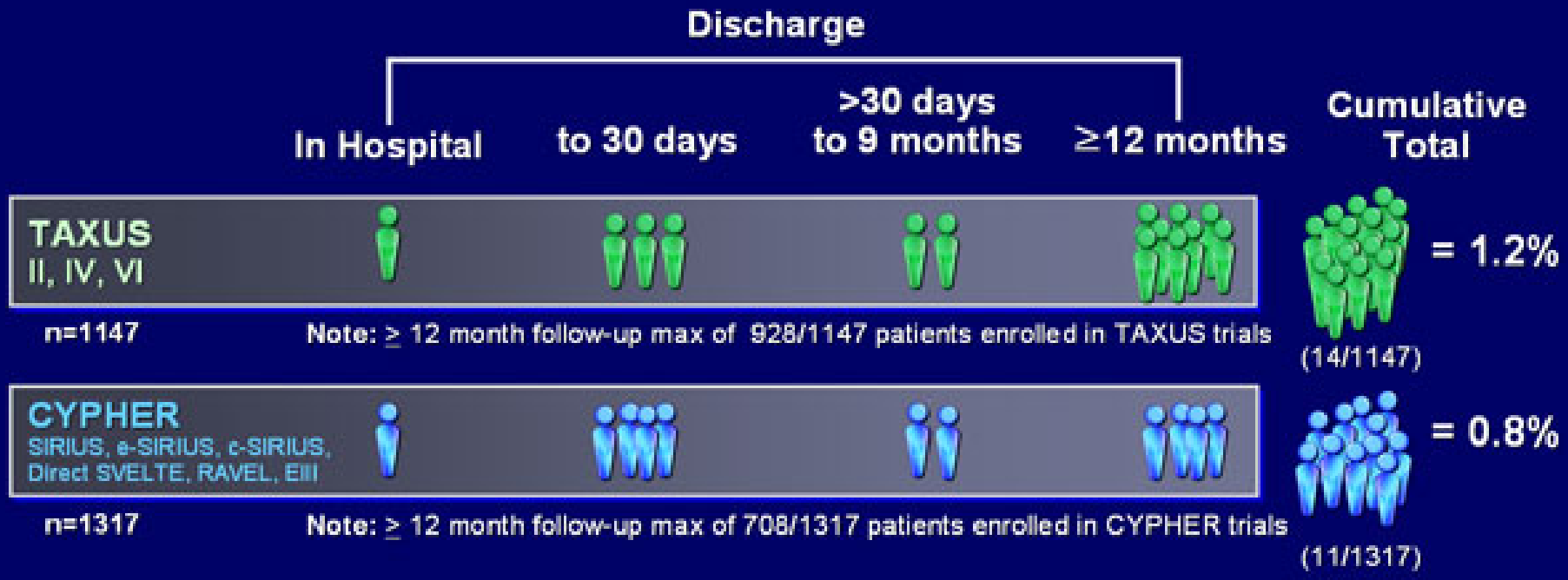
Combined Rates of Late Stent Thrombosis



Sources:
Taxus clinical trial and registry summary, BSX; *NEJM* Vol. 349, No. 14; J. Moses presentation ACC 04.
Cordis analyst meeting March 6, 2005 at ACC05; *LANCET* Vol 362, Oct 4, 2003.
***NEJM* Vol 346 No. 23; Leon SIRIUS 3-year update ACC 05.**
ESC Congress 2005 – Drug-eluting stents bare metal stents: still an issue in 2005?

ENDEAVOR Clinical Trial Program

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Conclusion

- The Endeavor stent is highly deliverable
- The need for repeat intervention is low and maintained
- No stent thromboses were observed beyond 10 days
- These clinical data confirm that the Endeavor stent is a safe, effective and durable treatment option for patients undergoing PCI in the DES era

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Conclusion

ENDEAVOR clinical program supports sustained clinical efficacy and outstanding safety results in these moderately complex lesion subsets