ENDEAVOR III

12-month Clinical Trial Results and Overview of Zotarolimus/PC/Cobalt Technology and Clinical Trial Program

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No conflicts of interest to declare

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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 8/9 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.

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Study Objectives

- **To determine if the 8 month angiographic outcomes (in-segment late loss) of the Endeavor DES are non-inferior to the FDA-approved Cypher DES**

- **To determine if the results of the Endeavor DES in a United States patient population (ENDEAVOR III) are similar to those obtained in the ENDEAVOR II pivotal clinical trial conducted outside the United States**

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Multicenter randomized trial

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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: 18–33 mm (8/9) mm bailout
Pre-dilatation required

n=436 patients
30 U.S. sites

Endeavor Stent
n=327

Cypher Stent
n=109

Clinical/MACE

Clinical Endpoints

30d | **6mo** | **8mo** | **9mo** | **12mo** | **2yr** | **3yr** | **4yr** | **5yr**

Angio/IVUS

QCA
IVUS

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 Zotarolimus per mm stent length

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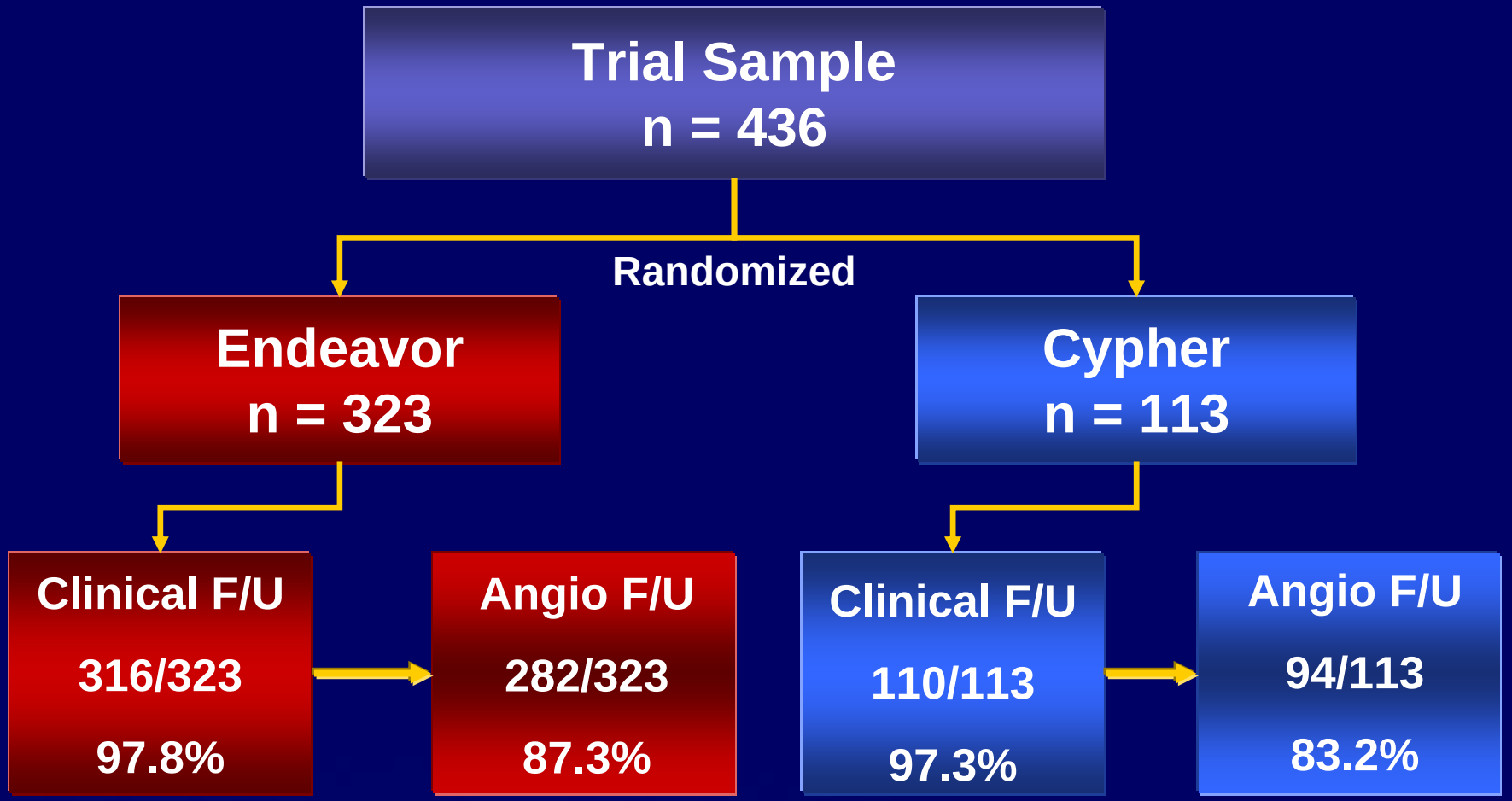
Patient Flowchart



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Patient Demographics

	Endeavor n = 323	Cypher n = 113	*P* value
Male Gender (%)	65.3	81.4	0.001
Age (years)	61.4±10.6	61.7±11.6	0.80
Prior MI (%)	19.9	20.7	0.89
Prior PCI (%)	22.6	16.8	0.23
Diabetes Mellitus (%)	29.7	28.3	0.81
Unstable Angina (%)	51.1	55.7	0.48
Hyperlipidemia (%)	83.5	86.7	0.46
History of Smoking (%)	66.5	75.2	0.10

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Baseline Angiography

	Endeavor n = 323	Cypher n = 113	*P* value
LAD (%)	41.3	39.8	0.82
B2/C Lesions (%)	67.4	56.6	0.05
RVD (mm)	2.75	2.79	0.49
Lesion Length (mm)	14.98	14.95	0.96
Pre-procedure MLD (mm)	0.92	0.90	0.60
Post-index procedure			
In-Stent MLD (mm)	2.67	2.67	1.00
In-Stent Acute Gain (mm)	1.75	1.77	0.74
In-Stent DS (%)	4.4	5.9	0.14
In-Segment MLD (mm)	2.26	2.28	0.82
In-Segment DS (%)	19.4	20.2	0.55

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Procedure Characteristics

	Endeavor n = 323	Cypher n = 113	*P* value
Number of Stents/Pt	1.1	1.2	0.28
Total Stent Length (mm)	22.3	23.0	0.40
Stent:Lesion Length	1.7	1.7	0.42
Stent diameter			0.19
2.5 mm (%)	23.7	15.9	
3.0 mm (%)	38.6	45.8	
3.5 mm (%)	37.7	38.3	
Max Inflation (ATM)	13.5	14.5	<0.001
GP IIb/IIIa Inhibitor (%)	44.0	44.6	0.91

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Procedure Results

	Endeavor n=323	Cypher n=113	*P* value
Device Success (%)	98.8	94.7	0.02
Procedure Success (%)	98.1	91.2	0.002

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

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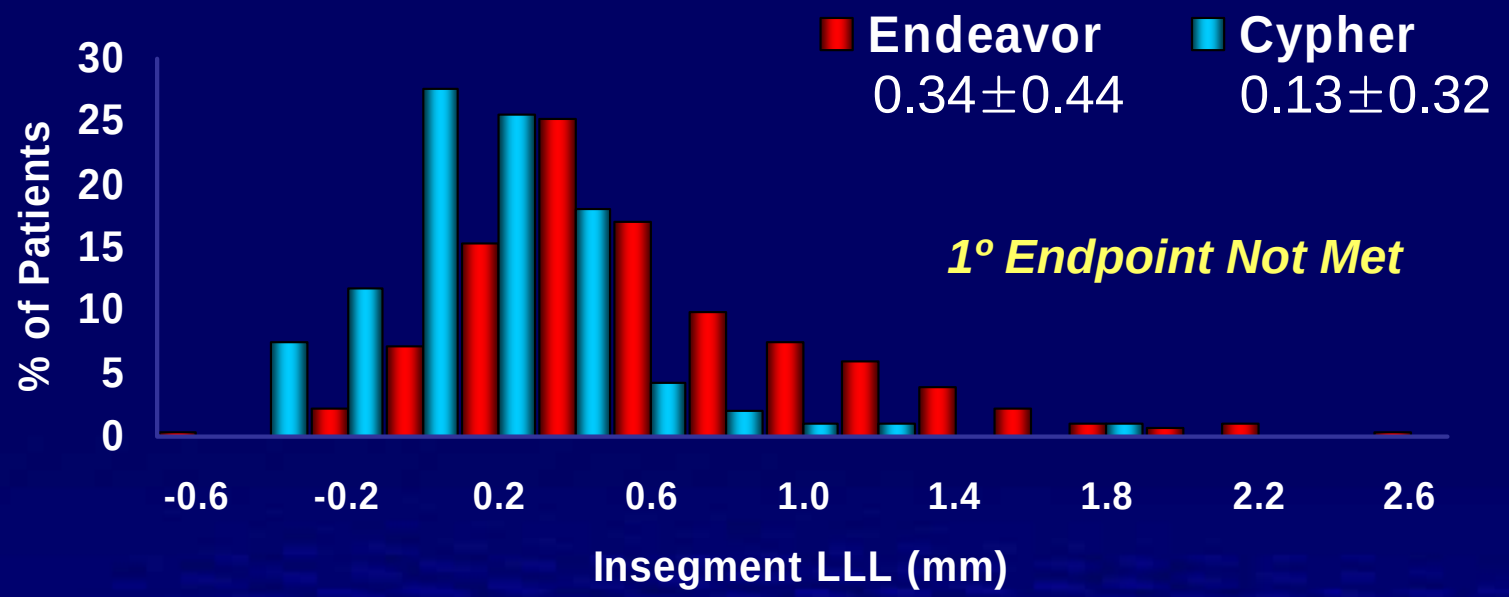
Primary Endpoint In-segment LL

- **Non-Inferiority Margin of Difference: 0.20 mm**
  - *90% Power, 5% α-one sided*
- **Observed Difference: 0.21 mm**



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Angiographic and IVUS results at 8 months

		Endeavor n = 282	Cypher n = 94	*P* value
Angiographic f/u % (N)		87.3	83.2	0.27
RVD (mm)		2.74	2.84	0.07
MLD (mm)	In-Stent	2.08	2.52	<0.001
	In-Segment	1.92	2.16	<0.001
DS (%)	In-Stent	24.3	11.0	<0.001
	In-Segment	29.9	23.9	<0.001
BAR (%)	In-Stent	9.2	2.1	0.02
	In-Segment	11.7	4.3	0.04
Late Loss (mm)	In-Stent	0.60	0.15	<0.001
	In-Segment	0.34	0.13	<0.001
Volume Obstruction (%)		16.1	2.7	<0.001
Late Incomplete Apposition (%)		0.5	5.9	0.02

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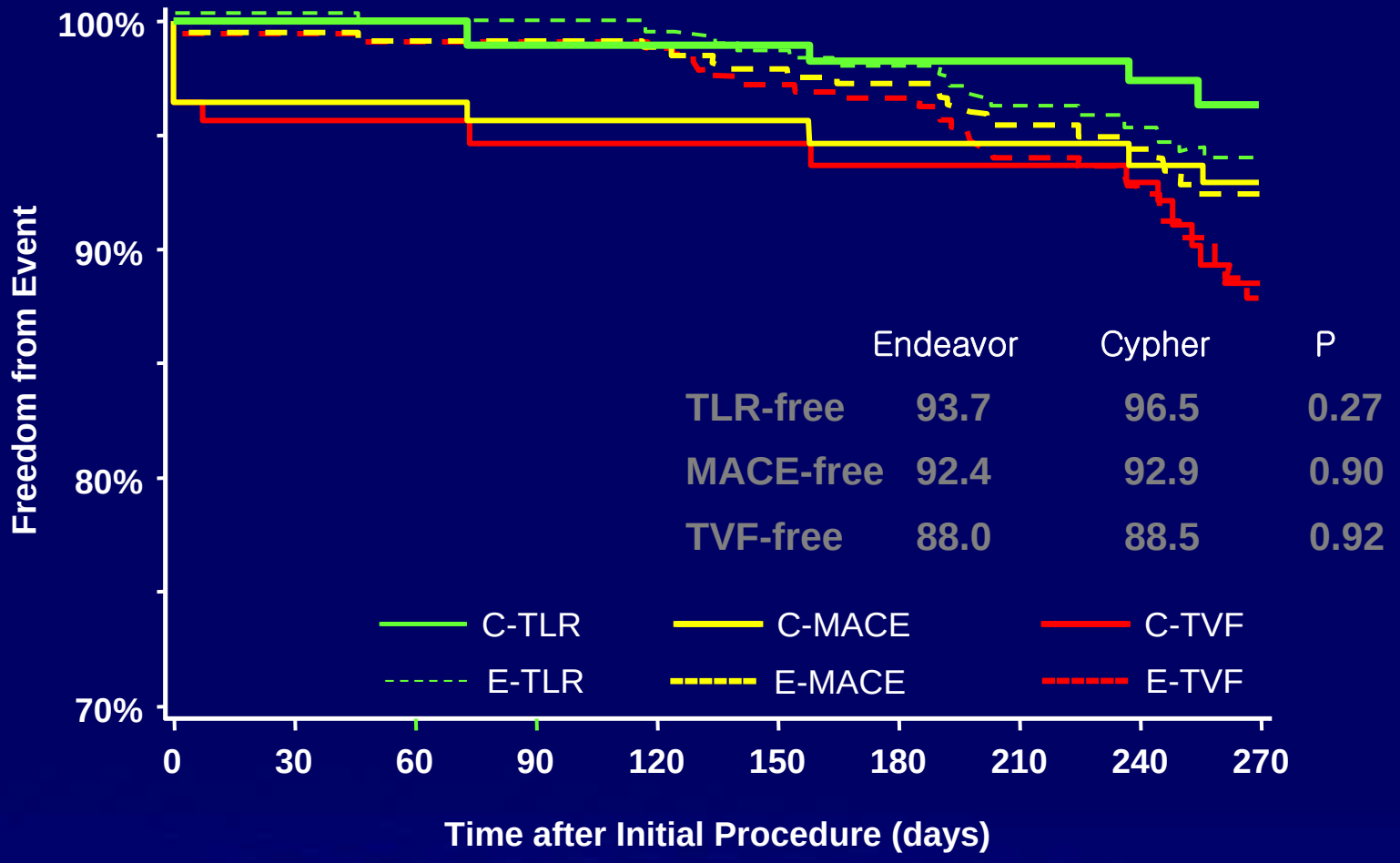
Event Free Survival at 9 months



	Endeavor	Cypher	P
TLR-free	93.7	96.5	0.27
MACE-free	92.4	92.9	0.90
TVF-free	88.0	88.5	0.92

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Clinical Results at 9 months

	Endeavor n = 316	Cypher n = 113	*P* value
MACE (%)	7.6 (24)	7.1 (8)	1.00
Death	0.6 (2)*	0	1.00
Q-Wave MI	0	0	--
Non Q-Wave MI	0.6 (2)	3.5 (4)	0.04
CABG	0	0	--
TLR	6.3 (20)	3.5 (4)	0.34
CABG	0.9 (3)	0	0.57
PCI	5.4 (17)	3.5 (4)	0.61
Stent Thrombosis (%)	0	0	--
TVR (non-TL) (%)	6.0 (19)	5.3 (6)	1.00
TVF (%)	12.0 (38)	11.5 (13)	1.00

** Non cardiac deaths (lung cancer, cerebral hemorrhage)*

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Clinical Results at 12 Months

	9-12 mos Endeavor n = 316	12 mos Endeavor n=316	9-12 mos Cypher n = 110	12 mos Cypher n=110	*P* value
MACE (%)	2	8.2 (26)	1	8.2 (9)	1.00
Death	–	0.6 (2)*	1	0.9	1.00
Q-Wave MI	–	0	–	0	–
Non Q-Wave MI	–	0.6 (2)	–	3.6 (4)	0.04
CABG	–	0	–	0	–
TLR	2	6.9 (22)	–	3.6 (4)	0.25
Stent Thrombosis (%)	–	0	–	0	–
TVR (non-TL) (%)	2	6.6 (21)	–	5.5 (6)	0.82
TVF (%)	2	13.2 (42)	1	11.8 (13)	0.87

*Non cardiac deaths (lung cancer and cerebral hemorrhage).

ENDEAVOR Clinical Program

Overview of Clinical 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	28.9
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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Study	ENDEAVOR Combined (n=1,306)
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**

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Clinical Outcomes

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	9.7

*EI 12-month results. Data represented as percentages

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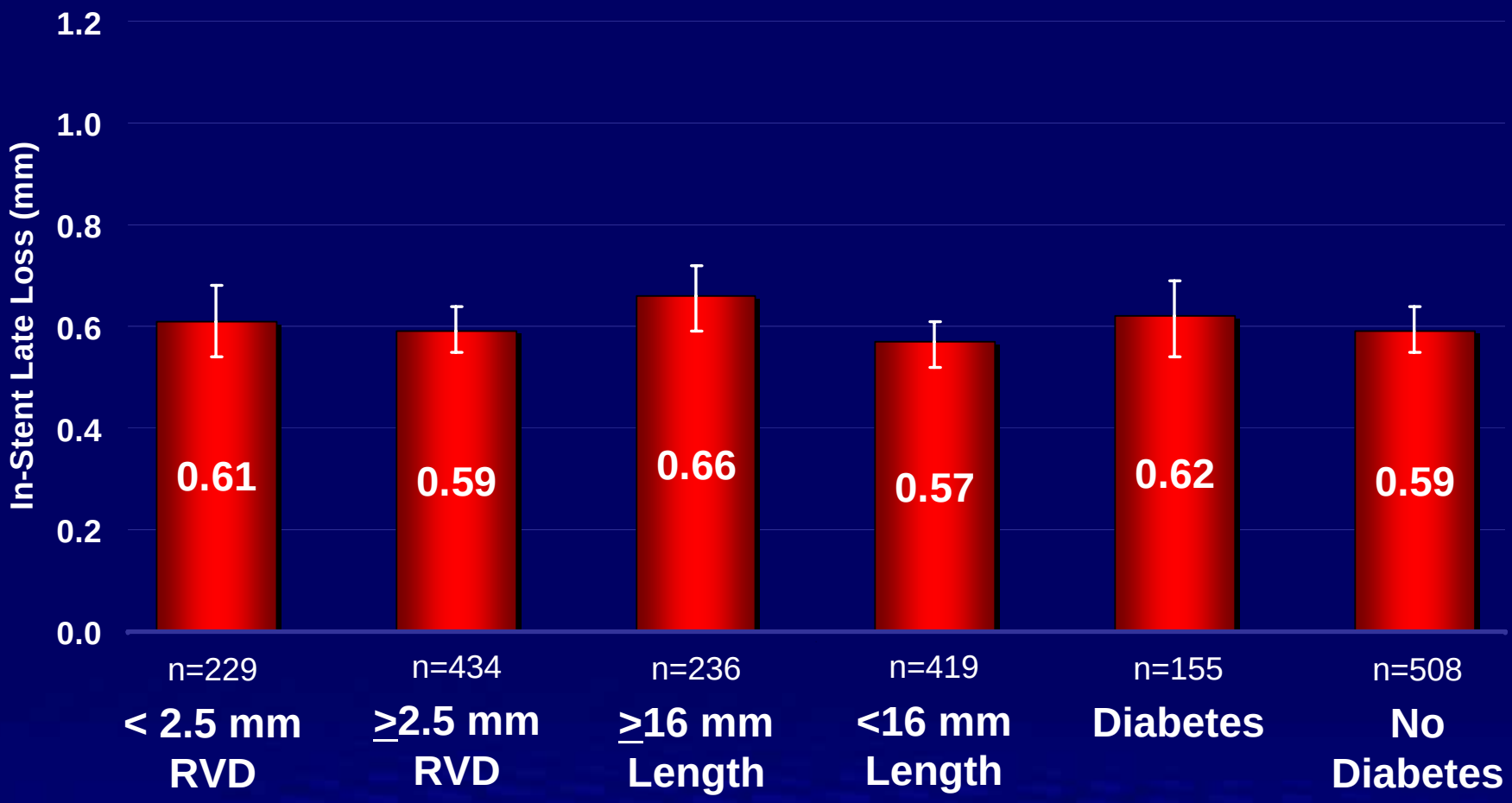
LL Across High Risk Subgroups



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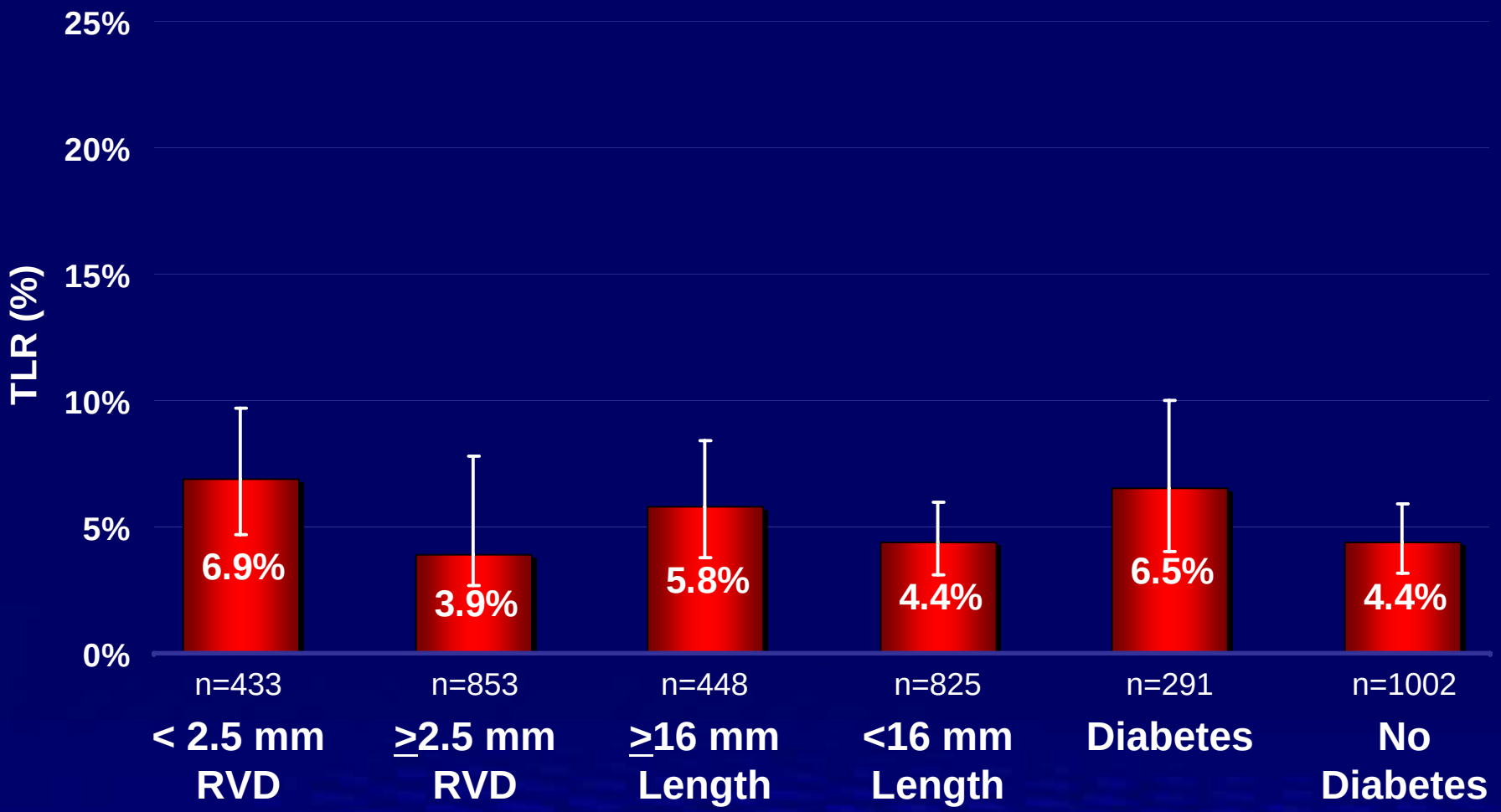
TLR Rates Across High Risk Subgroups



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Stent Thrombosis Rate

	0-30 days	30-365 days	>365 days
EI (100)	1%	0	0
EII (598)	0.5%	0	0
EII CA (296)	0	0	—
EIII (323)	0	0	—
Overall (1317)	0.3%	0%	—

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Conclusions

- The non-inferiority primary endpoint of in-segment late loss was not met
- No significant differences in 12 month clinical outcomes (TLR, MACE, TVR and TVF)
- Improved device success (deliverability) and lower in-hospital and 30-day MACE (NQWMI) resulted in a significant difference in procedure success favoring Endeavor
- Endeavor: Consistency in clinical and angiographic outcomes across broader patient, lesion and physician subset