ENDEAVOR II
A Randomized Trial to Evaluate the Safety and Efficacy of the Medtronic AVE ABT-578 Eluting Driver Coronary Stent in De Novo Native Coronary Artery Lesion

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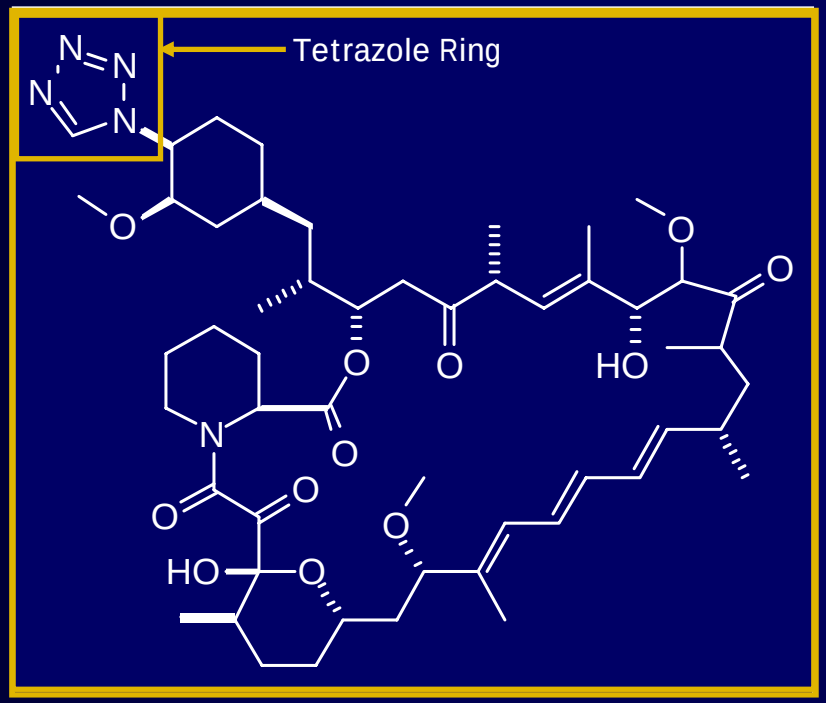
for the Endeavor II investigators

***no conflicts of interest**

ABT-578



Unique, patent-protected molecule discovered and synthesized at Abbott Laboratories

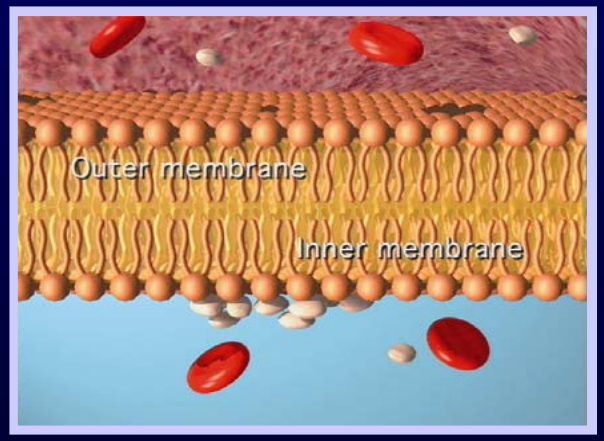
Structurally different from rapamycin through the substitution of a tetrazole ring at the 42- position with opposite stereochemistry

Endeavor DES System

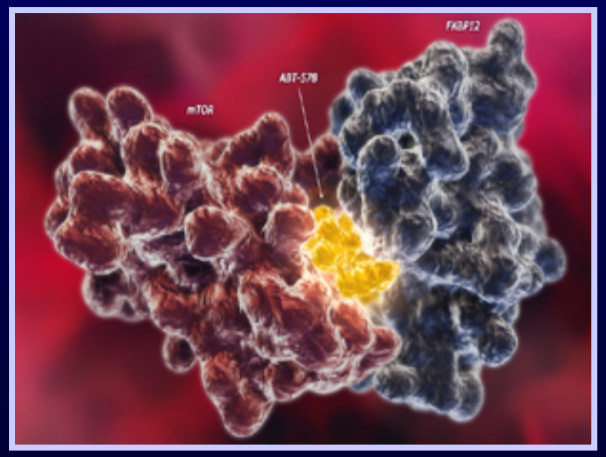
Driver Cobalt Alloy Stent

Stent Delivery System

PC Technology

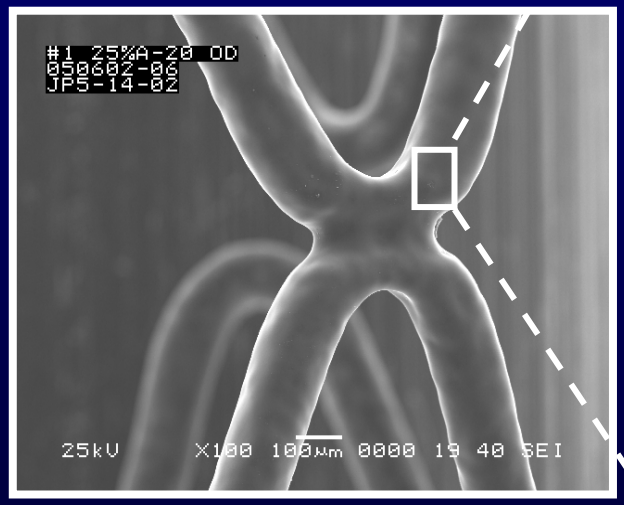


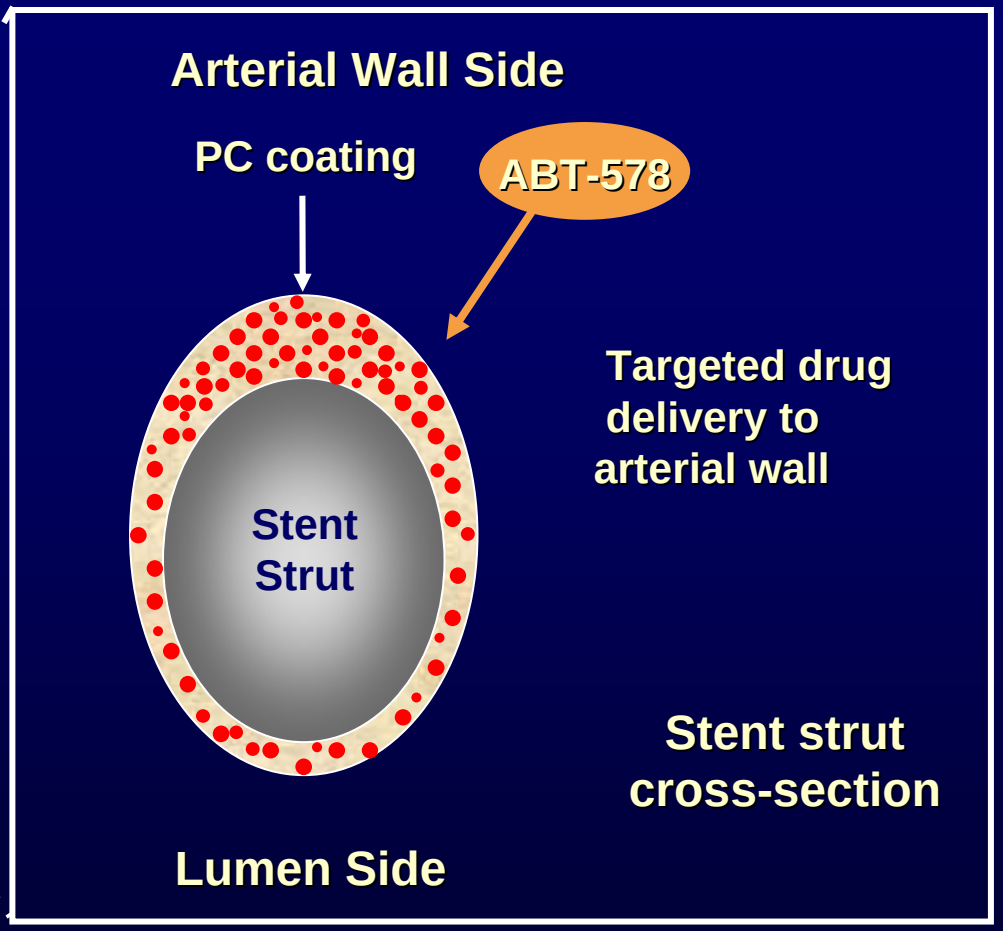
Drug: ABT-578



Endeavor ABT-578 Eluting Stent

ABT-578 and PC polymer are applied on the Driver stent with a proprietary manufacturing process

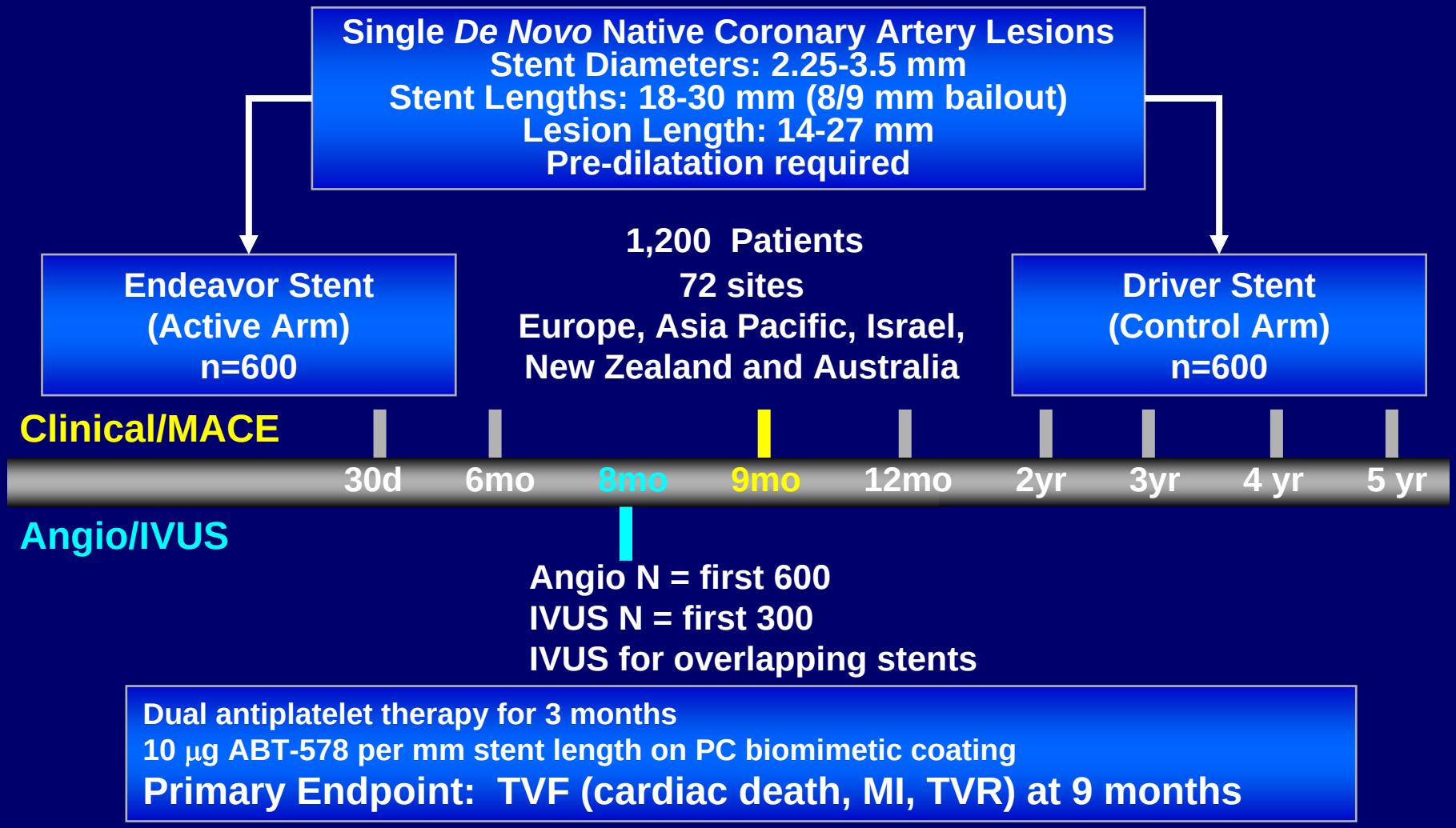




Endeavor Clinical Program

Trial	Design	N
Endeavor I	Registry	100
Endeavor II	RCT Endeavor vs Driver (1:1)	1197
Endeavor III	RCT Endeavor vs Cypher (3:1)	436
Endeavor IV	RCT Endeavor vs Taxus (1:1)	1548
Continued Access EII	Registry	300

ENDEAVOR II
Randomized, Double-Blind Trial Design



ENDEAVOR II
Power Calculations for Primary Endpoint

We assumed a reduction in 9-month target vessel failure rate from 16.0% to 9.5% (~40% treatment effect)

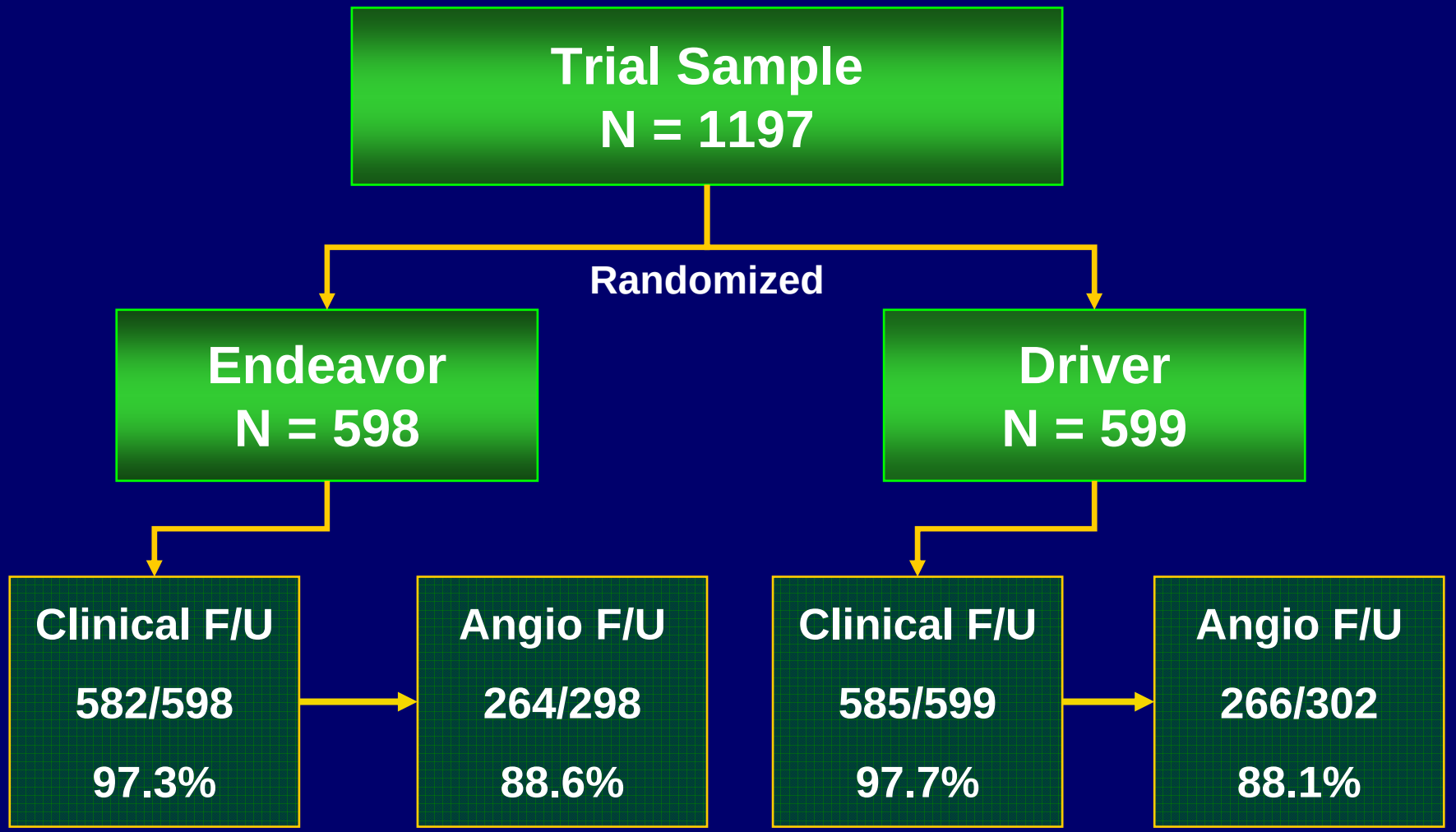
The power of the study was 90%

The two-sided alpha error was 5%

The calculated sample size was 552 subjects per arm, or 1104 required evaluable subjects

A total of 1200 patients was enrolled to account for errors in the assumptions and for subjects lost to follow-up

ENDEAVOR II
Patient Flowchart



Core Laboratories

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Cardiovascular Core Analysis Lab
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Peter Fitzgerald, MD

ECG Core Lab
Harvard Clinical Research Institute, Boston, MA, USA
Peter Zimetbaum, MD

Data Coordinating Center
Harvard Clinical Research Institute
Ralph D'Agostino, PhD

Clinical Events Committee/DSMB
Harvard Clinical Research Institute, Boston, MA, USA
Donald Cutlip, MD

ENDEAVOR II

Key Inclusion/Exclusion Criteria

Inclusion

- Planned single-vessel, single de novo lesion intervention
  - Reference vessel diameter 2.25-3.5 mm
  - Lesion length 14-27 mm
  - Diameter stenosis ≥ 50% and < 100%
  - No other significant lesions in the target vessel
- Ethics Committee approved written informed consent

Exclusion

- Congestive heart failure, renal insufficiency
- Known and relevant hypersensitivities
- AMI within 72 hrs
- Any PCI (past or planned) within 30 days of randomization
- History of anti-restenotic therapy (e.g., DES, IVRT)
- Evidence of thrombus in the target vessel
- Excessively tortuous vessel
- Significant (>50%) stenosis proximal or distal to the target lesion

ENDEAVOR II

Clinical Sites

Investigator	Hospital	Patients
G. Laarman	Onze Lieve Vrouwe Gasthuis, Amsterdam	66
K-H. Kuck	Krankenhaus Sankt Georg, Hamburg	54
J. Ormiston	Mercy Hospital, Auckland	54
T. Münzel	Universitätsklinikum, Hamburg-Eppendorf	47
E. Hauptmann	Krankenhaus der Barmherzigen Brüder, Trier	42
M. Suttorp	St. Antonius Ziekenhuis, Nieuwegein	41
J. Drzewiecki	Katowice University Hospital, Katowice	41
M. Pieper	Herzzentrum Bodensee, Kreuzlingen	37
H-P. Schultheiss	Universitätsklinikum Benjamin Franklin, Berlin	37
W. Ruzyllo	Institute of Cardiology Warsaw, Warsaw	33
P. Pieniazek	John Paul II Hospital, Krakow	33
H. Heuer	Medizinische Klinik St. Johannes, Dortmund	32
E. Grube	Krankenhaus & Herzzentrum, Siegburg	32
B. Hennen	Universitätskliniken des Saarlandes, Homburg	29
J. Bonnier	Catharina Ziekenhuis, Eindhoven	28
R. Kornowski	Beilinson Hospital, Petach Tikva	28
A. Zeiher	Klinikum der J-W Goethe, Frankfurt	27

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Clinical Sites (continued)

Investigator	Hospital	Patients
E. Camenzind	University Hospital, Geneva	25
R. Whitbourn	St. Vincents Hospital, Melbourne	21
C. Hamm	Kerckhoff Klinik, Bad Nauheim	20
W. Chan	National Heart Center, Singapore	20
A. Lekston	Slaskie Centrum Chorob Serca, Zabrze	19
W. Rutsch	Universitatsklinikum Charité, Berlin	18
C. Lotan	Hadassah University Hospital, Jerusalem	18
P. Kay	Dunedin Hospital, Dunedin	17
F. Schiele	CHU Jean Monjoz, Besancon	17
R. Simon	Universitatsklinikum, Kiel	16
W. Wijns	Onze Lieve Vrouw Ziekenhuis, Aalst	16
B. Lewis	Lady Davis Carmel Medical Center, Haifa	16
P. Sick	Universitat Leipzig Herzzentrum, Leipzig	16
D. Glogar	AKH Wein, Vienna	15
R. Beyar	Rambam Medical Center, Haifa	15
J. Motwani	Derriford Hospital, Plymouth	14
D. Muller	St. Vincents Hospital Sydney, Sydney	14

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Clinical Sites (continued)

Investigator	Hospital	Patients
I. Meredith	Monash Medical Center, Fitzroy Victoria	13
M. Vrolix	ZOL Campus St. Jan, Genk	13
O. Darremont	Clinique Saint-Augustin, Bordeaux	13
W. Jukema	Leiden University Medical Center, Leiden	12
P. Vermeersch	AZ Middelheim, Middelheim	12
L. Thuessen	Skejby Hospital, Arhus	11
R. Hoffmann	Medical Clinic University Aachen, Aachen	11
L. Michalis	University Hospital of Ioannina, Ionnina	11
D. Carrie	Hospital de Rangueil – CHU, Toulouse	10
F. Fajadet	Clinique Pasteur, Toulouse	10
F. Eberli	University of Zürich, Zürich	9
C. De Cock	AZVU, Amsterdam	8
C. Dubois	University Hospital Gasthuisberg, Leuven	8
J. Quininha	Hospital de Santa Marta, Lisbon	8
N. Uren	Royal Infirmary, Edinburgh	8
O. Kwok	Grantham Hospital, Hong Kong	7
C. Tan	National University Hospital, Singapore	7
A. Zaman	Freeman Hospital, Newcastle	7

ENDEAVOR II

Clinical Sites (continued)

Investigator	Hospital	Patients
J. Boland	Hospital de la Citadelle, Liege	6
F.J. Neumann	Herz-Zentrum, Bad Krozingen	6
G. Grollier	Centre Hospitalier Universitaire, Caen	6
O. Pachinger	LKH Innsbruck, Innsbruck	5
P. Richard	Centre Hospitalier Saint Martin, Caen	5
J.M. Juliard	Hospitalier Bichat-Claude Bernard, Paris	5
P. Henry	AP-HP Hoptial Lariboisiere, Paris	5
S. Silber	Private Praxis Muenchen	4
D. Crochet	Hospital Guillaume et Tene Laennel, Nantes	3
P. Coste	Hospital Cardiologique du Haut Leveaue, Pessac	3
H. Kelbaek	Righspitalet The Heart Centre, Copenhagen	2
A. Banning	John Radcliff Hospital, Oxford	2
Y. Louvard	Institute Hospitalier Jacques Cartier, Massy	2
K.D. Dawkins	Southampton General Hospital, Southampton	2
V. Guetta	Sheba Medical Center, Tel Hashomer	2
T. Gershlick	Glenfield Hospital, Leicester	2
V. Legrand	CHU Sart Tilman, Liege	1

Patients Demographics

	Endeavor N = 598	Driver N = 599	P value
Male Gender (%)	77.2	75.3	ns
Age (years)	61.6 ± 10.5	61.9 ± 10.5	ns
Prior MI (%)	39.7	41.5	ns
Prior PCI (%)	21.7	18.0	ns
Diabetes Mellitus (%)	18.0	22.2	ns
Unstable Angina (%)	30.3	30.3	ns
Recent MI (%)	16.1	14.5	ns
Hyperlipidemia (%)	80.5	76.9	ns
Current Smoker (%)	35.3	35.2	ns

Angiographic Characteristics

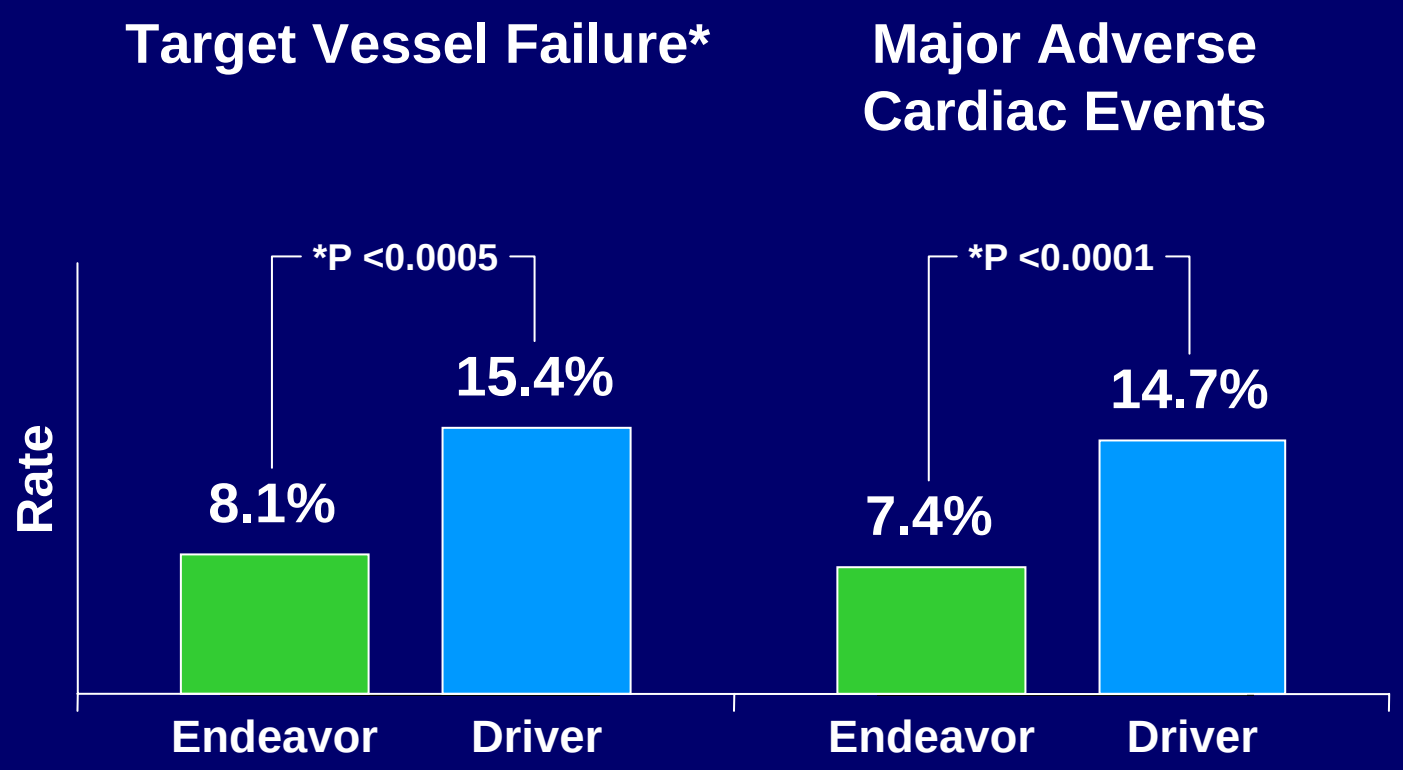
	Endeavor N = 598	Driver N = 599	P value
LAD (%)	43.4	47.5	ns
B2/C Lesions (%)	78.4	78.9	ns
RVD (mm)	2.74	2.76	ns
Lesion Length (mm)	14.05	14.39	ns
Stent Length (mm)	23.3	23.2	ns
Pre-procedure MLD (mm)	0.83	0.84	ns
Post-index procedure			
In-Stent MLD (mm)	2.59	2.61	ns
In-Stent Acute Gain (mm)	1.76	1.77	ns
In-Stent DS (%)	6.1	6.3	ns
In-Segment MLD (mm)	2.21	2.24	ns
In-Segment DS (%)	20.6	20.2	ns

Procedure Characteristics

	Endeavor N = 588	Control N = 589	P Value
Stent Length:Lesion Length	1.84	1.79	ns
Stents per Lesion	1.12	1.11	ns
IIb/IIIa inhibitor use	13.2%	10.4%	ns
Lesion Success	99.8%	100%	ns
Device Success	99.3%	99.3%	ns
Procedure Success	97.4%	97.1%	ns

Lesion success	<50% residual in-segment percent diameter stenosis
Device success	<50% residual in-segment percent diameter stenosis with assigned stent
Procedure success	<50% residual in-segment percent diameter stenosis with assigned stent and without 30-day MACE

Clinical Outcomes
Primary Endpoint at 9 Month Follow-up



*Target Vessel Failure is a composite of target vessel revascularization, Q- or non Q-wave MI, or cardiac death

Clinical Results to 9 months

	Endeavor N = 582	Control N = 585	P value
Composite MACE (%)	7.4	14.7	<0.0001
Death	1.2	0.5	ns
Q-Wave MI	0.3	0.9	ns
Non Q-Wave MI	2.4	3.1	ns
CABG	0.0	0.0	ns
TLR	4.6	12.1	<0.0001
CABG	0.3	0.5	ns
PCI	4.3	11.6	<0.0001
TVR (%)	5.7	12.8	<0.0001
TVF (%) (Primary endpoint)	8.1	15.4	<0.0005

Endeavor II

9 month mortality

	Endeavor n = 582	Control n = 585	*P* value
Death	7 (1.2%)	3 (0.5%)	0.22
Cardiac*	5	3	
Non-Cardiac	2	0	

*Defined as death due to myocardial infarction, cardiac perforation or tamponade, arrhythmia, stroke within 30 days of the procedure or related to the procedure, death due to a complication of the procedure, and any death in which a cardiac cause cannot be excluded, as adjudicated by blinded clinical events committee.

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MDS 9m MACE Table 4

Endeavor II

*9 month cardiac mortality**

Treatment	Post-procedure day	Cause
Endeavor	1	Subacute stent thrombosis
Control	38	Acute respiratory failure
Control	92	Non-target vessel Q wave infarction
Control	134	Sudden death
Endeavor	175	Sudden death
Endeavor	182	Sudden death
Endeavor	229	Sudden death
Endeavor	243	Surgical death 1d post TLR-CABG

***As adjudicated by blinded clinical events committee.**

Endeavor II

*9 month non-cardiac mortality**

Treatment	Post-procedure day	Cause
Endeavor	39	Metastatic lung cancer
Endeavor	262	Intracerebral hemorrhage

***As adjudicated by blinded clinical events committee.**

Angiographic and Clinical Complications

9 Month Follow-up

	Endeavor (N=582)	Driver (N=585)
CVA	0.2% (1)	0.5% (3)
Major Bleeding	1.2% (7)	2.2% (13)
Vascular	0.5% (3)	1.2% (7)
Perforation*	0.5% (3)	0.3% (2)

*both clinical and angiographic included

p = ns for all comparisons

Safety Results

Stent Thrombosis	Endeavor N = 582	Driver N = 585	P value
In-hospital	0.3% (2)	0.3% (2)	
Discharge to 30 days	0.2% (1)	0.9% (5)*	
>30 – 270 days	0	0	
Total at 270 days	0.5% (3)	1.2% (7)	0.34

IVUS Results	Endeavor N = 100	Driver N = 83	P value
Late Acquired Stent Malapposition	0%	0%	ns
Late Aneurysm	0%	0%	ns

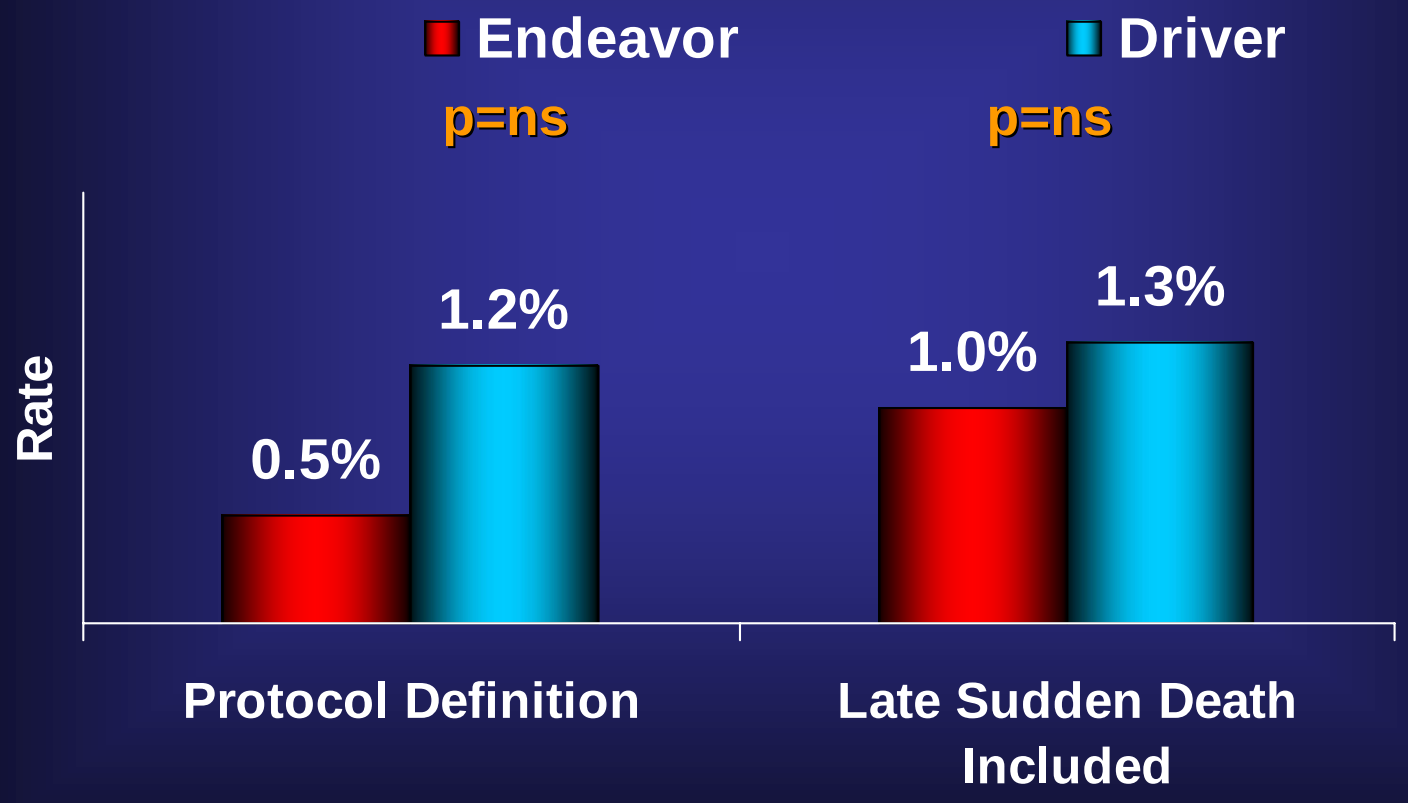
Stent thrombosis defined as angiographic thrombus or subacute closure in the stented vessel or any death not attributed to a non-cardiac cause within the 1st 30 days

*3/6 post-discharge stent thrombosis cases occurred in Driver arm when Plavix was stopped prematurely

Endeavor II

Stent Thrombosis Rates

Protocol Definition vs. Late Sudden Death Inclusive



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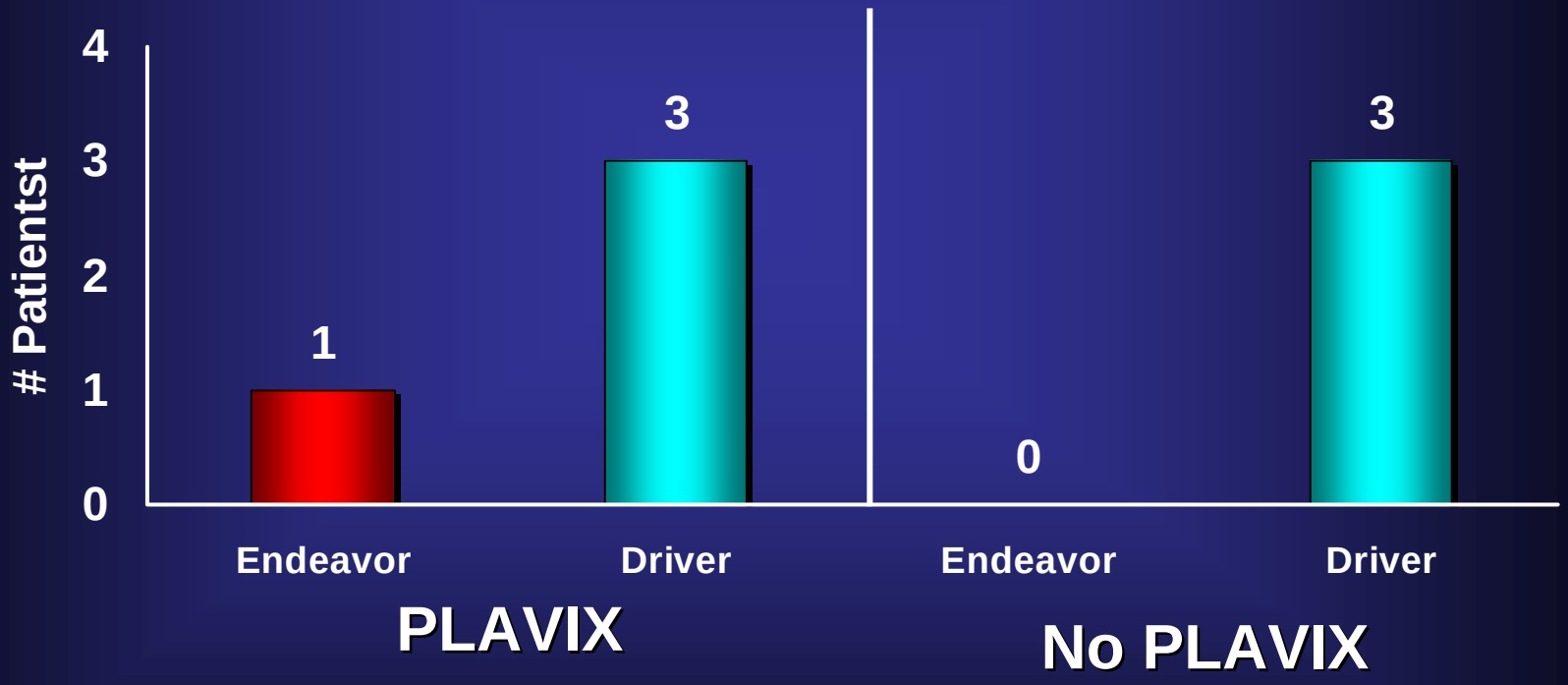
Stent Thrombosis and Plavix Use After > 1 Day



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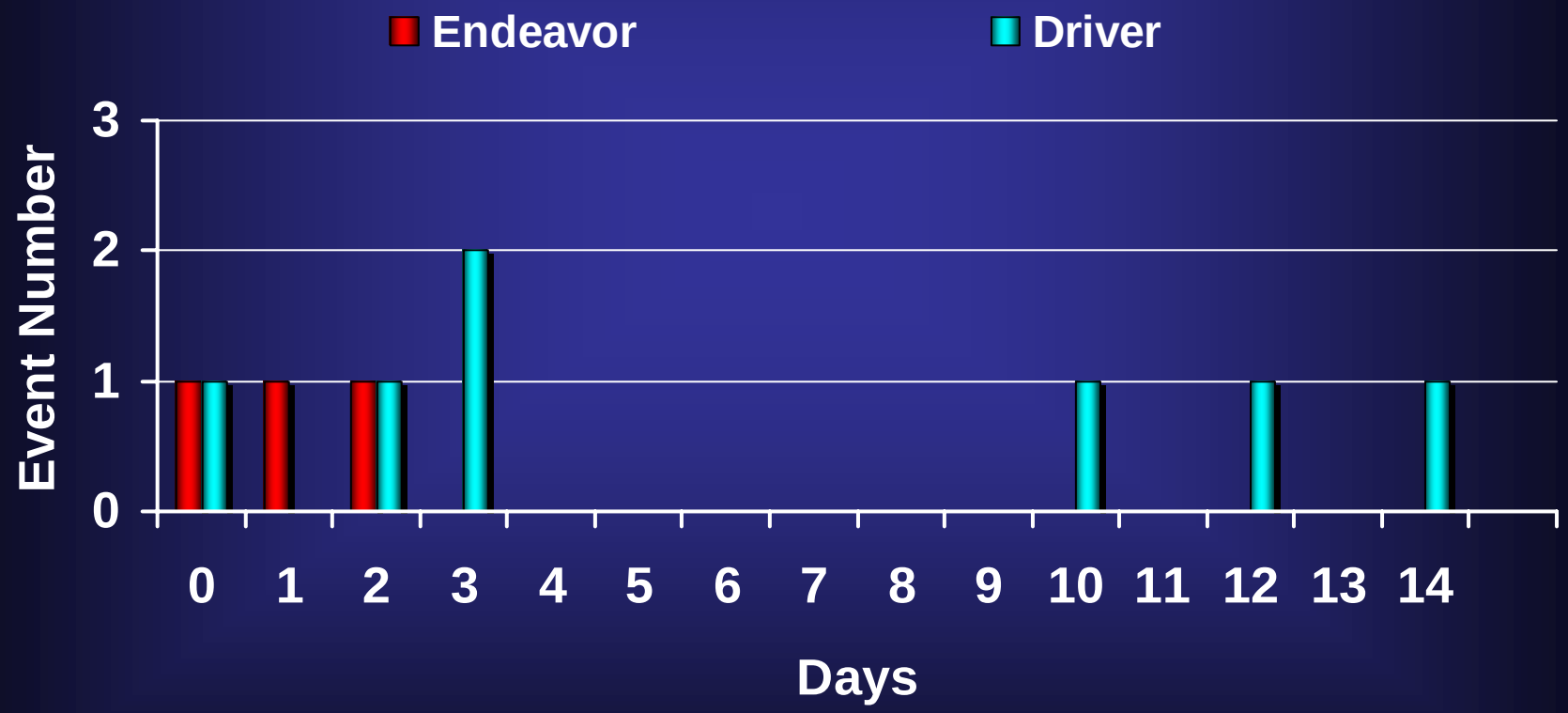
Stent Thrombosis Timing



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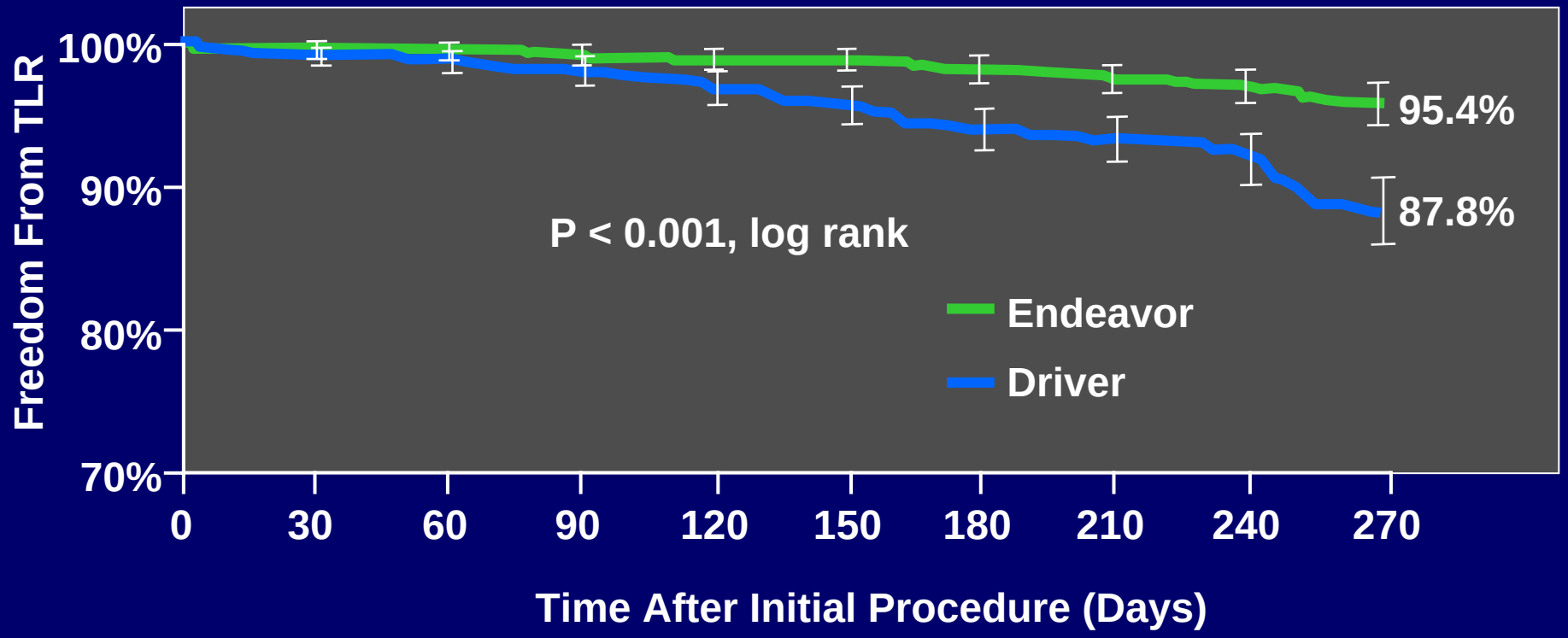
TLR-Free Survival



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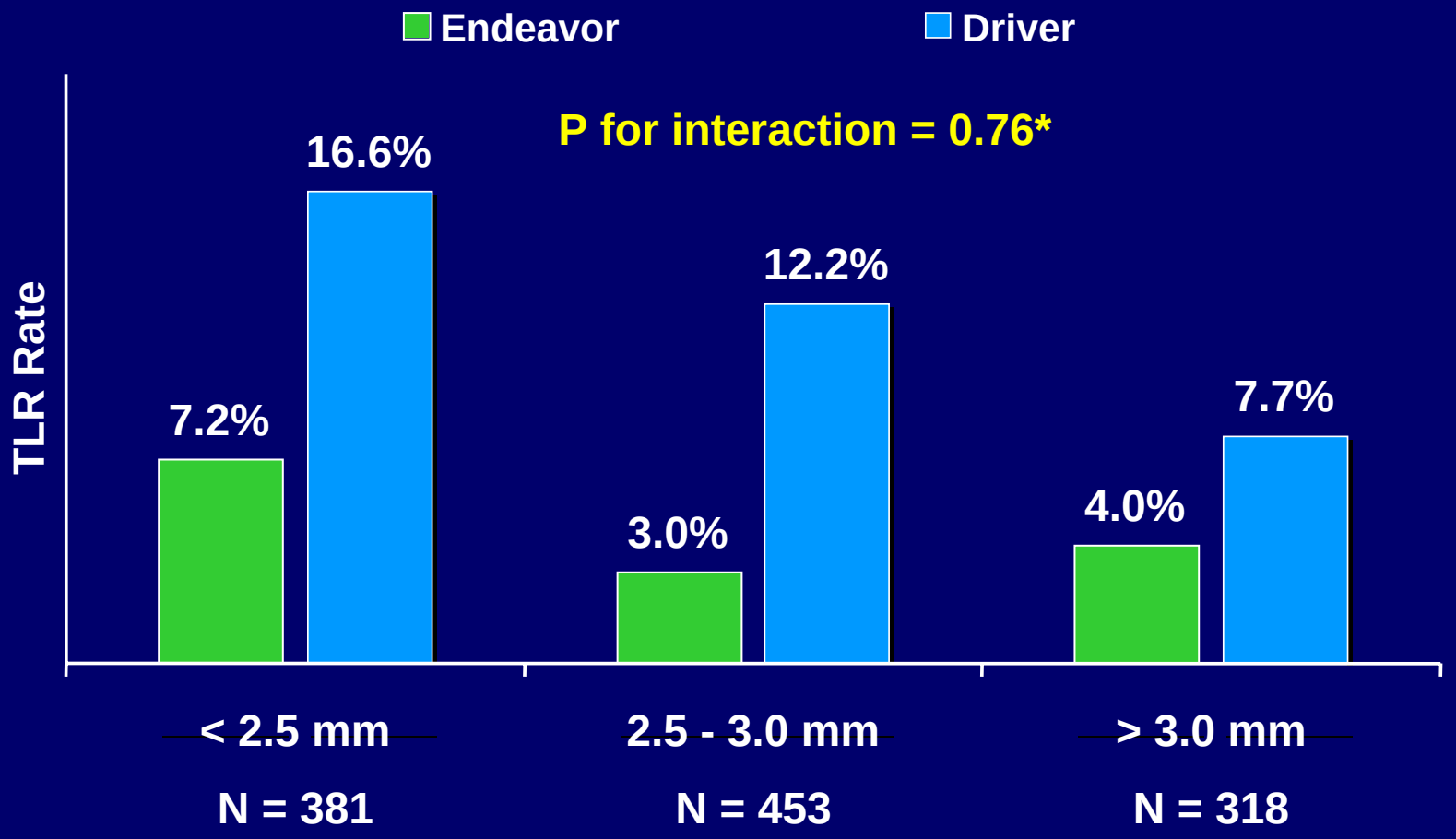
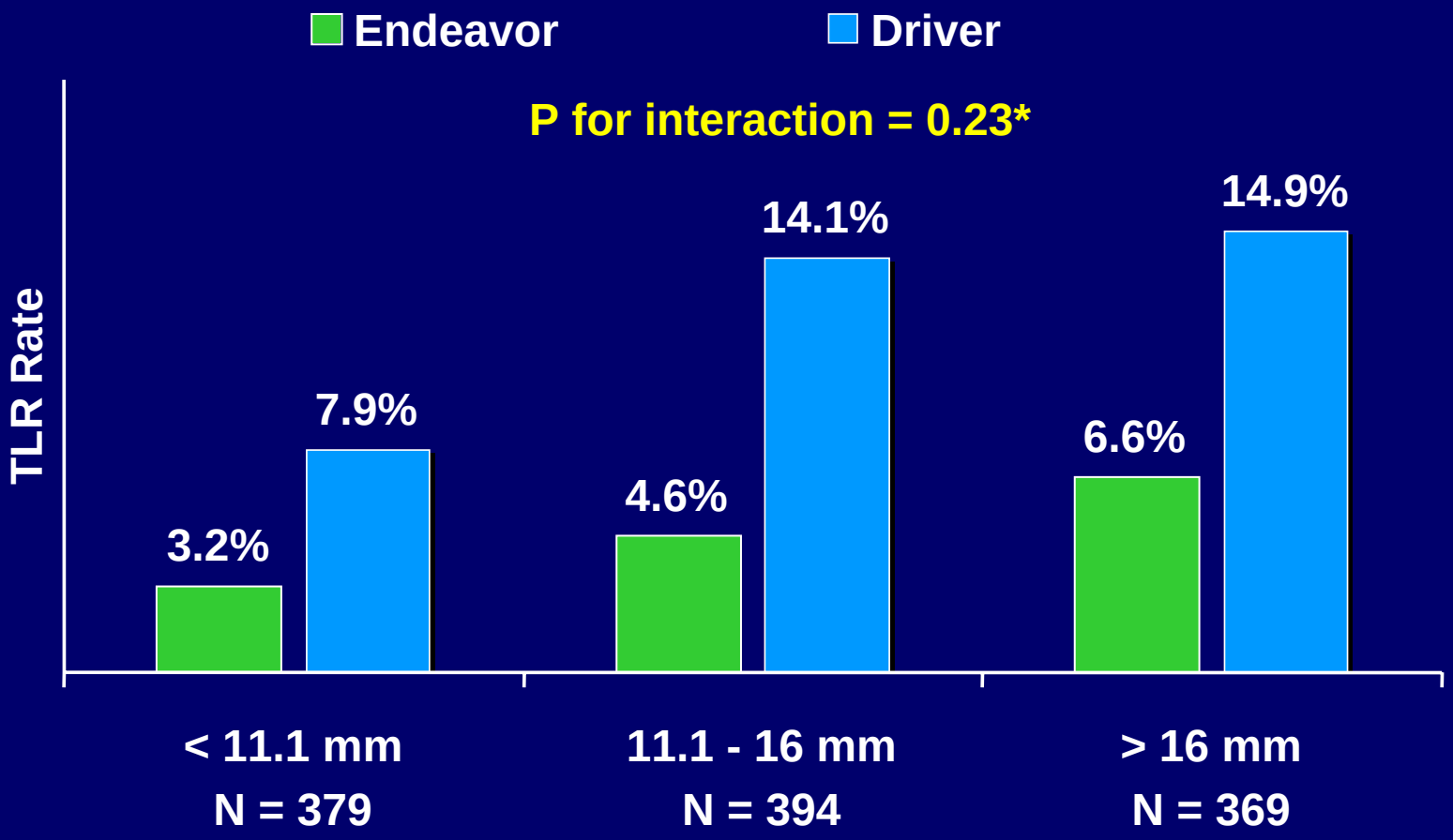
Vessel Size Subset Analysis
Target Lesion Revascularization



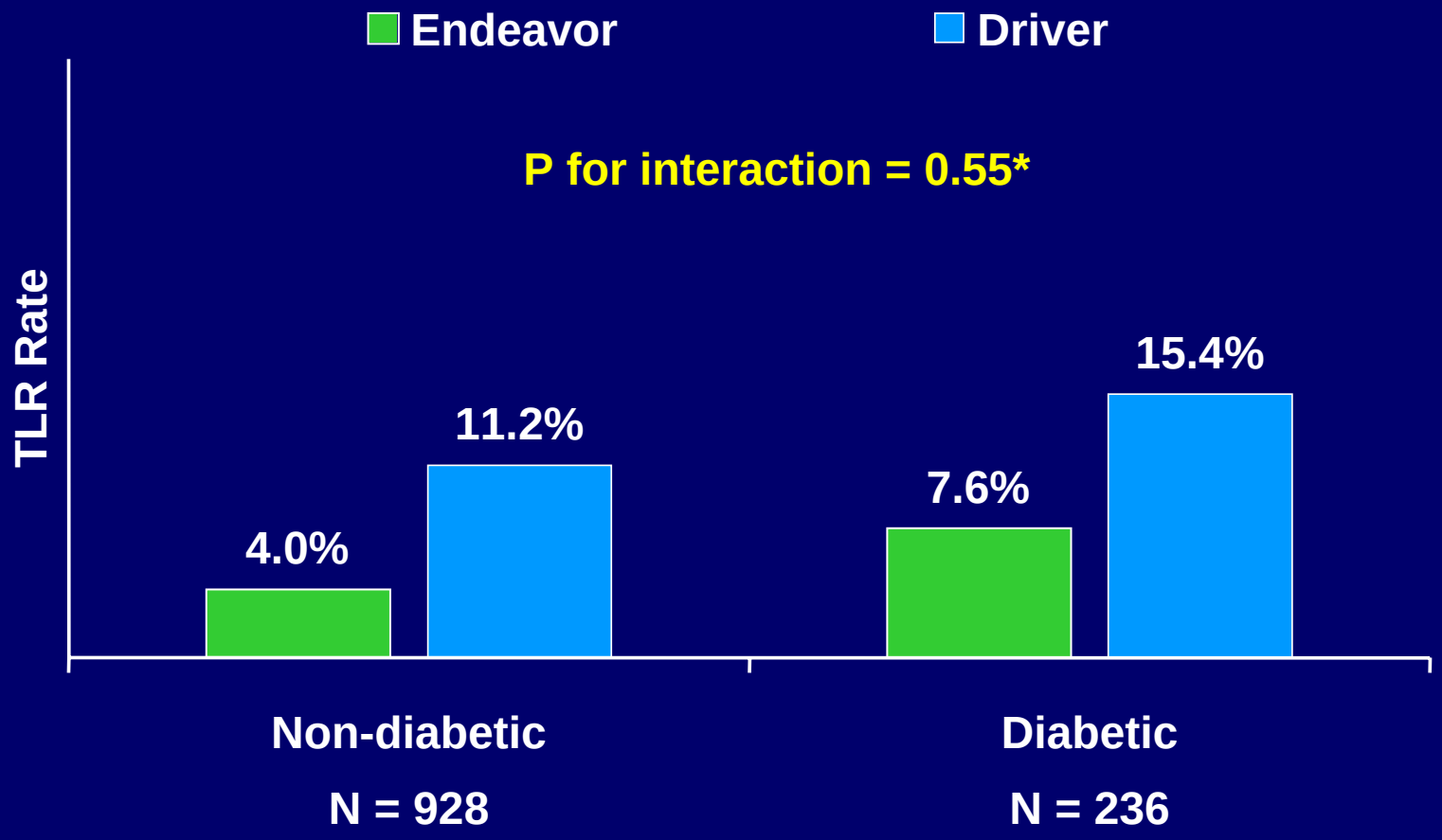
*Non-significant interaction p-value demonstrates uniform treatment effect across different vessel sizes

Lesion Length Subset Analysis
Target Lesion Revascularization



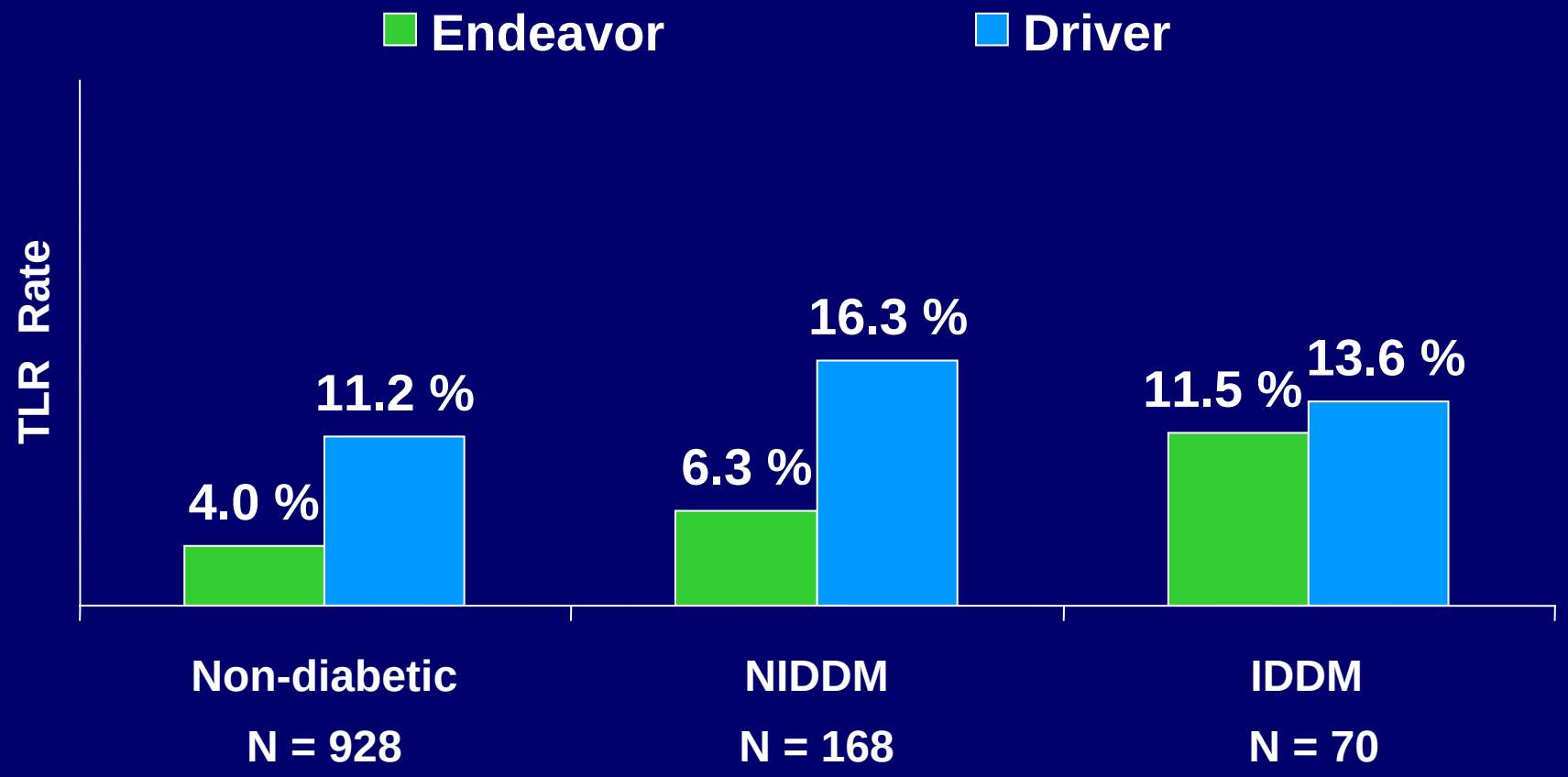
*Non-significant interaction p-value demonstrates uniform treatment effect across different lesion lengths

Diabetic Subset Analysis
Target Lesion Revascularization



*Non-significant interaction p-value demonstrates uniform treatment effect across diabetic and non-diabetic patients

Target Lesion Revascularization by Diabetes Type and Treatment



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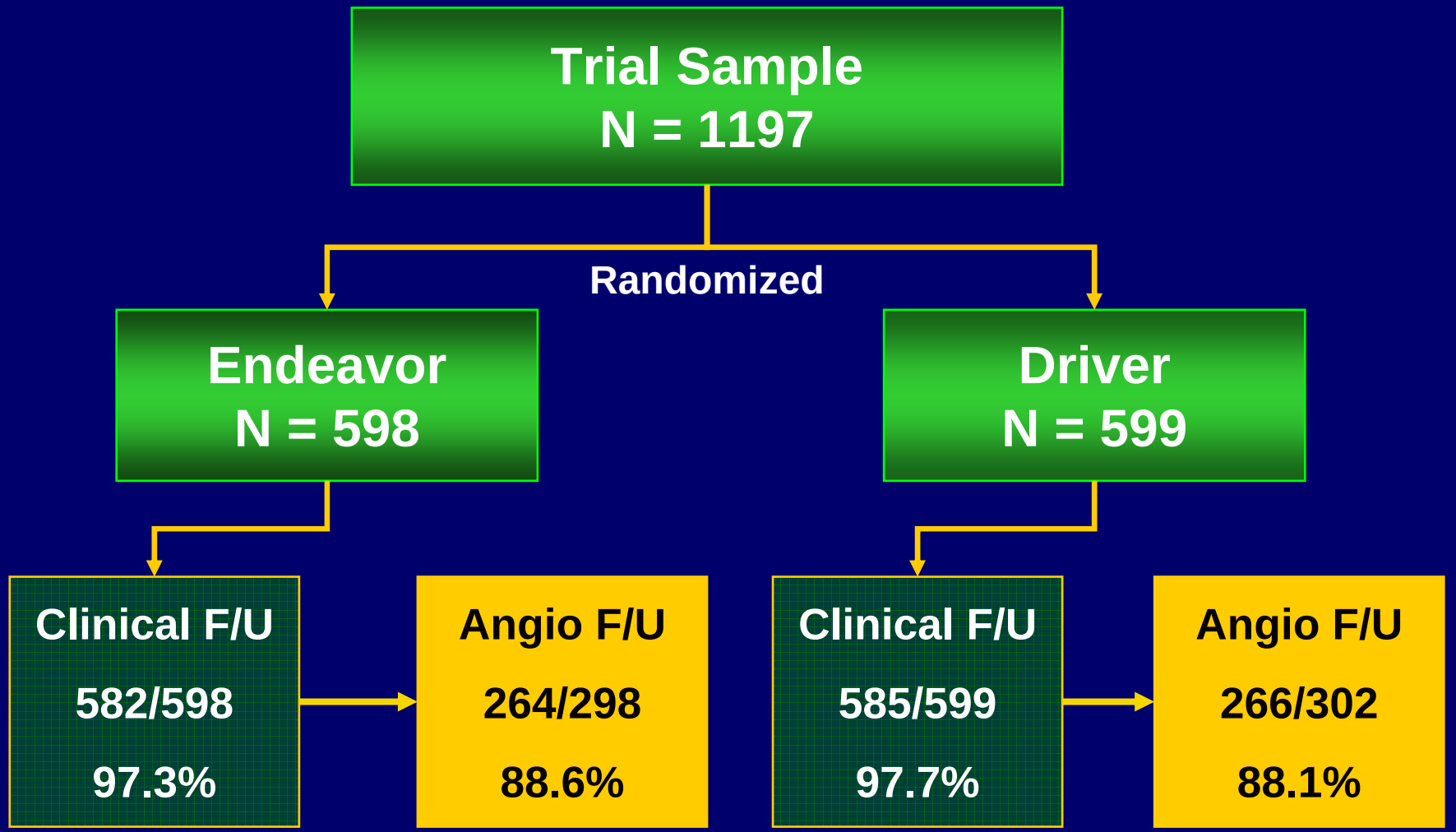
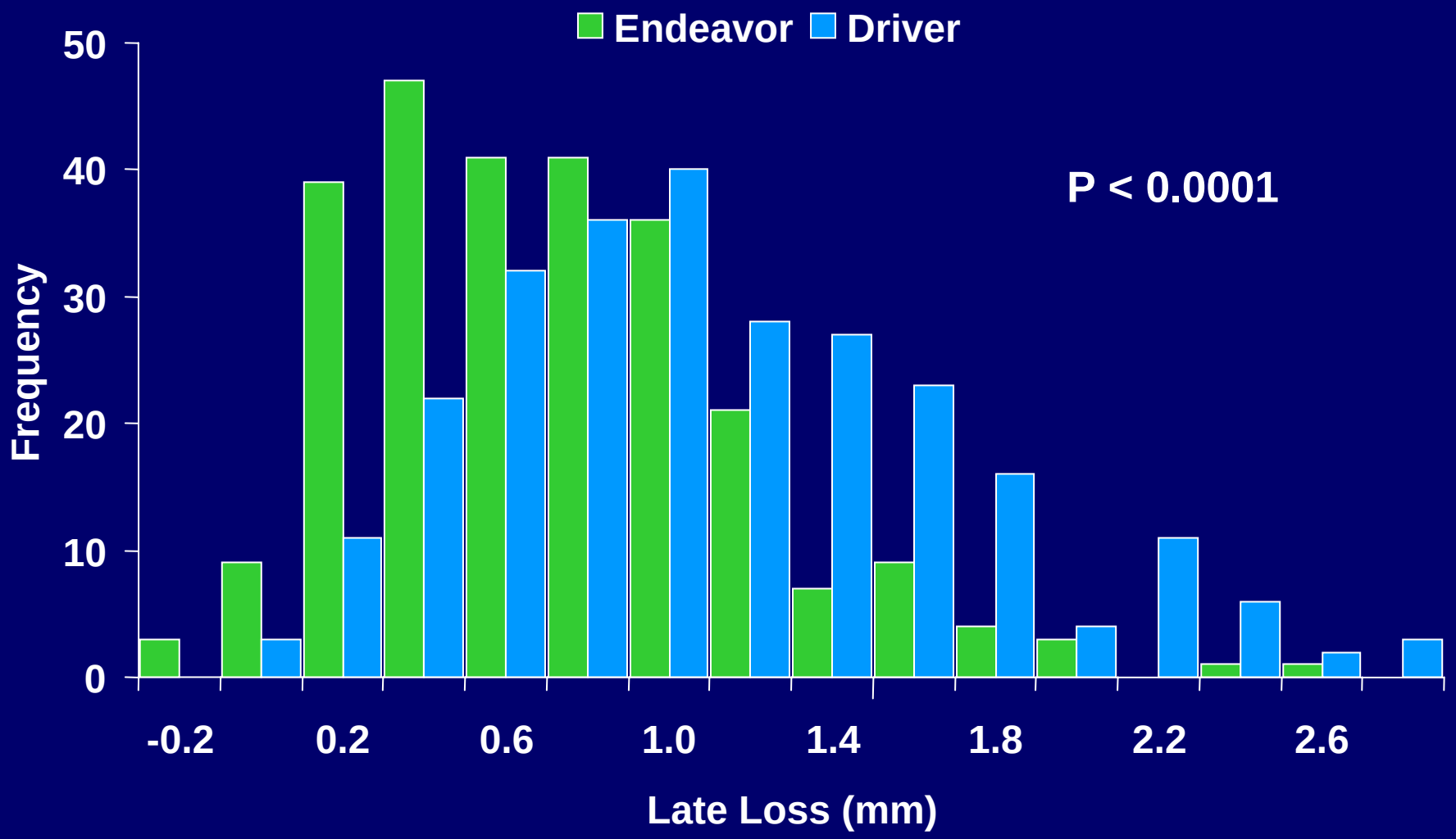
Patient Flowchart



Angiographic Results at 8 months

		Endeavor N = 298	Driver N = 302	P value
Follow-up % (N)		88.6 (264)	88.1 (266)	
RVD (mm)		2.75	2.78	0.39
MLD (mm)	In-Stent	1.99	1.63	<0.0001
	In-Segment	1.86	1.57	<0.0001
Diameter stenosis (%)	In-Stent	27.9	42.1	<0.0001
	In-Segment	32.6	44.3	<0.0001
Binary restenosis (%)	In-Stent	9.5	32.7	<0.0001
	In-Segment	13.3	34.2	<0.0001
Late Loss (mm)	In-Stent	0.62	1.03	<0.0001
	In-Segment	0.36	0.71	<0.0001
In-Stent LL index (regression)		0.34	0.54	

Distribution of In-Stent Late Loss



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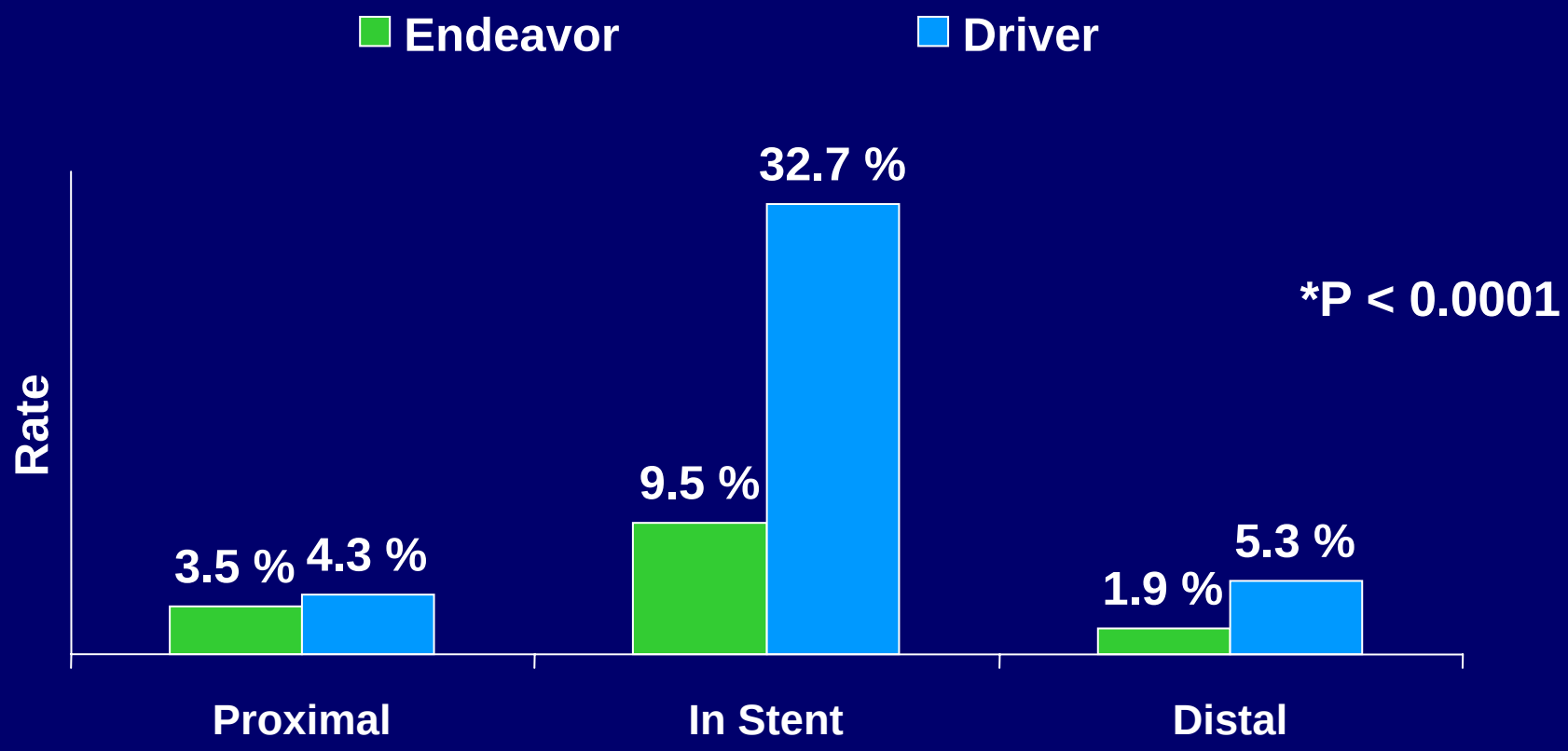
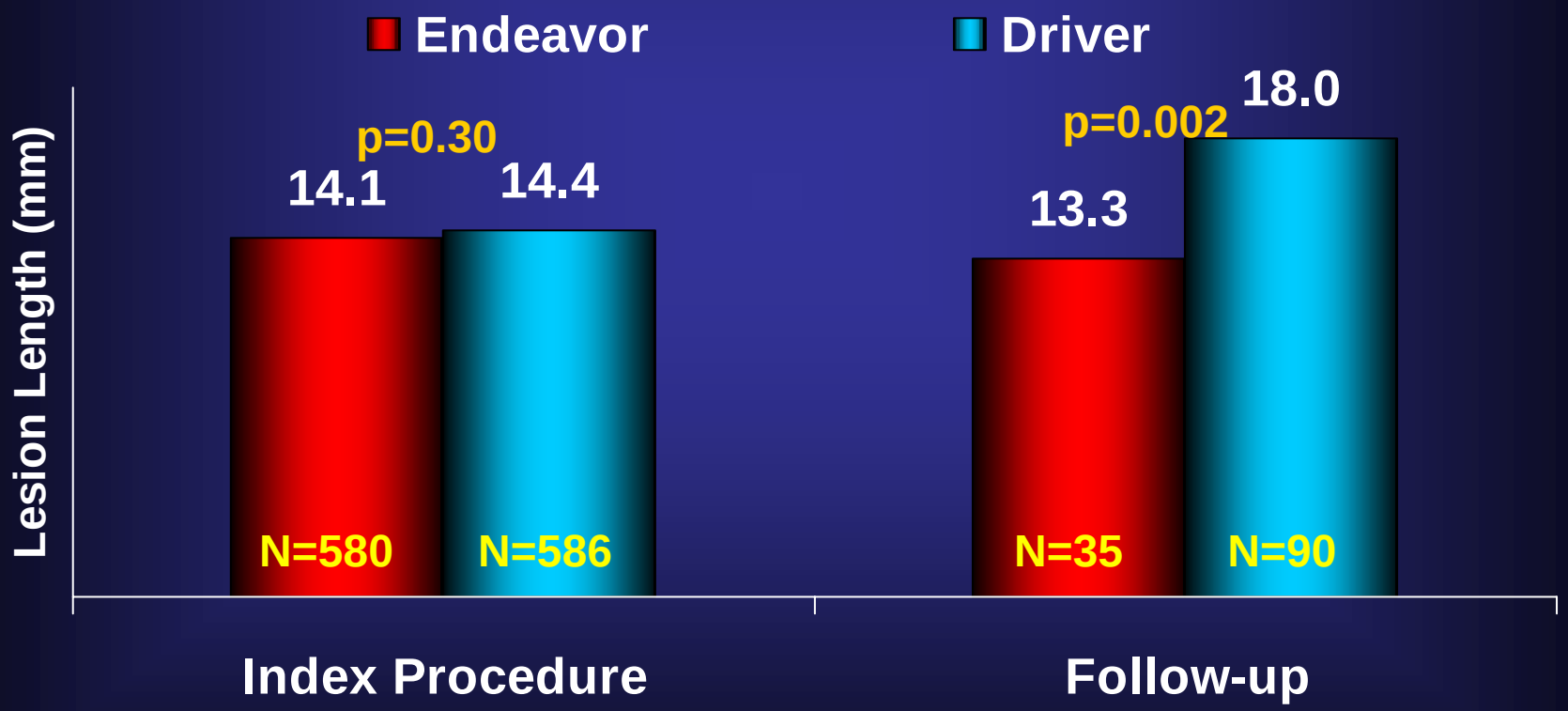
Patterns of Restenosis
Binary Restenosis Rate by Location



Endeavor II

Lesion Length

Index Procedure (All Subjects) and Follow-up (Binary Restenosis Only)



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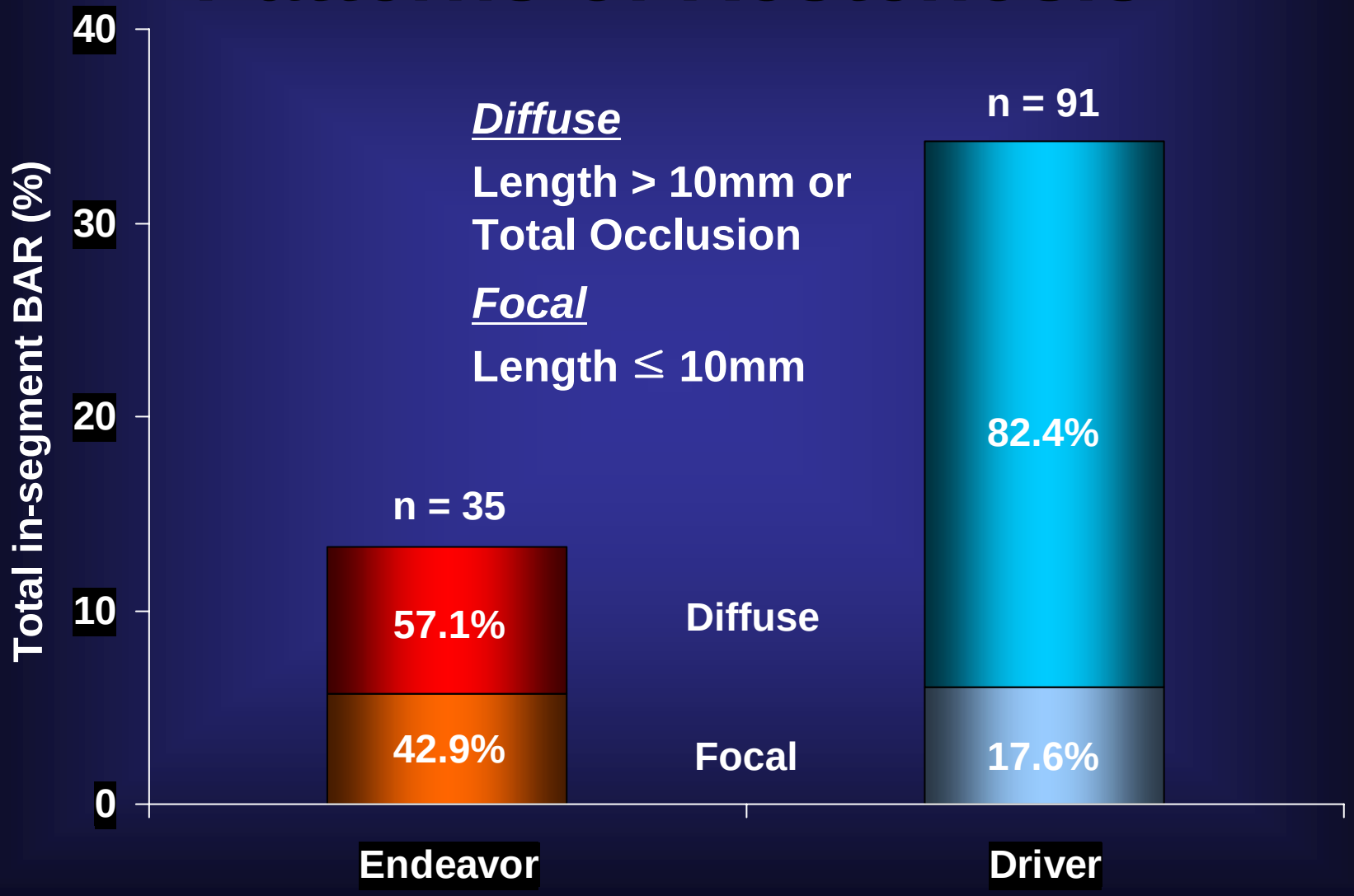
Endeavor II

Patterns of Restenosis



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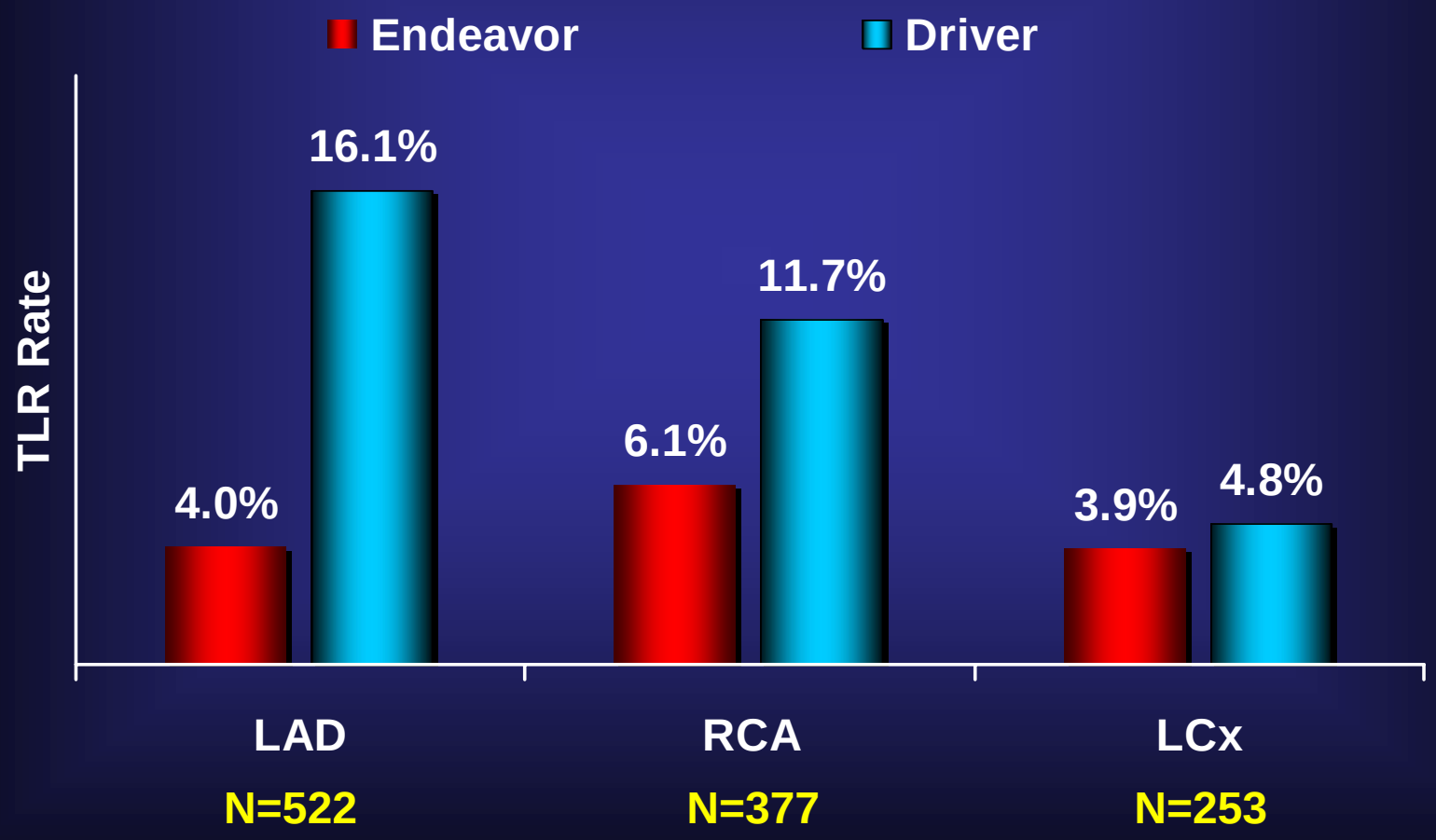
Subset Analyses

LAD Location

Endeavor II

TLR Rates by Lesion Location

LAD Subset Analysis



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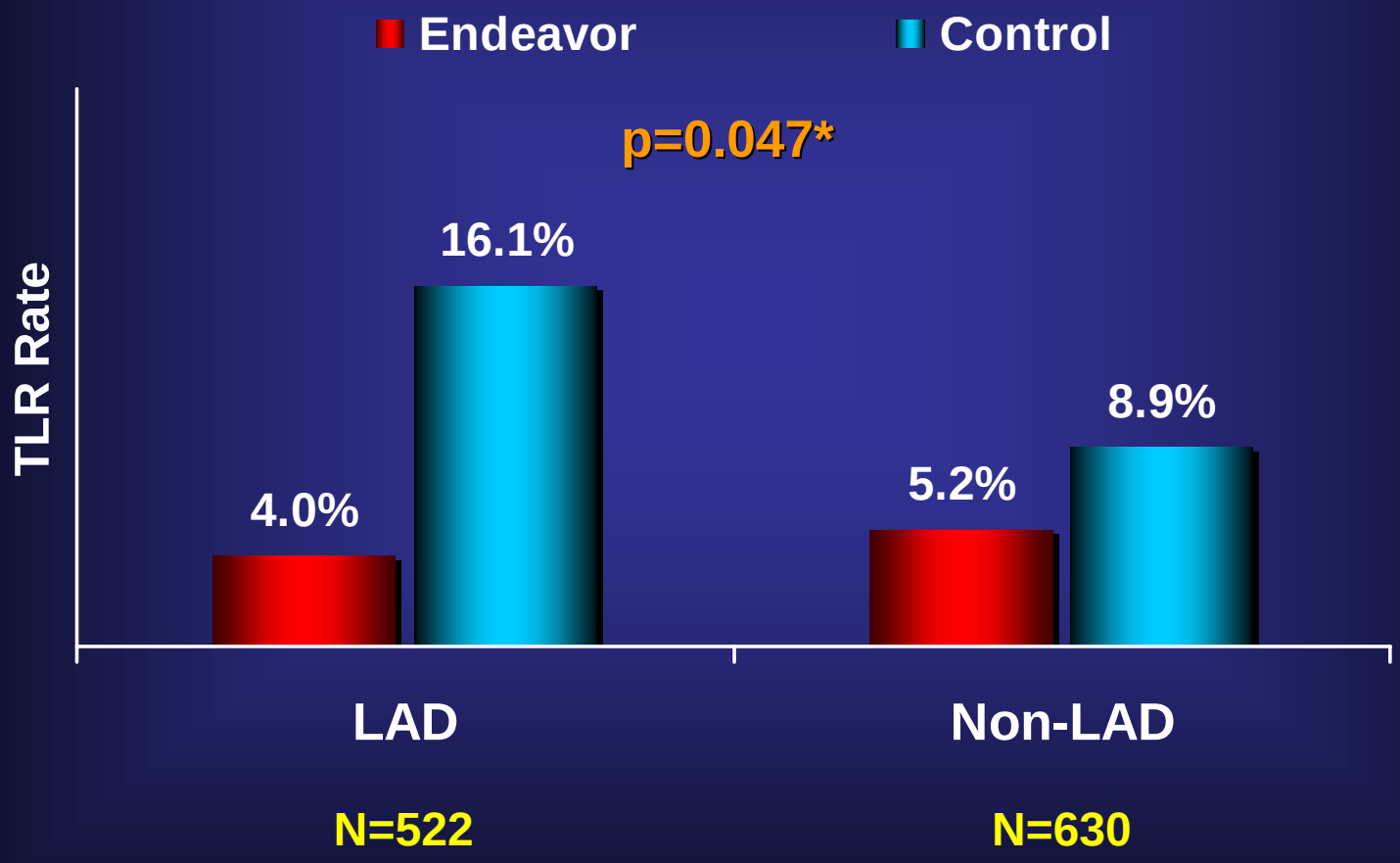
Target Lesion Revascularization

LAD Subset Analysis



Borderline LAD and TLR interaction p-value demonstrates a mild differential treatment effect for Endeavor and LAD

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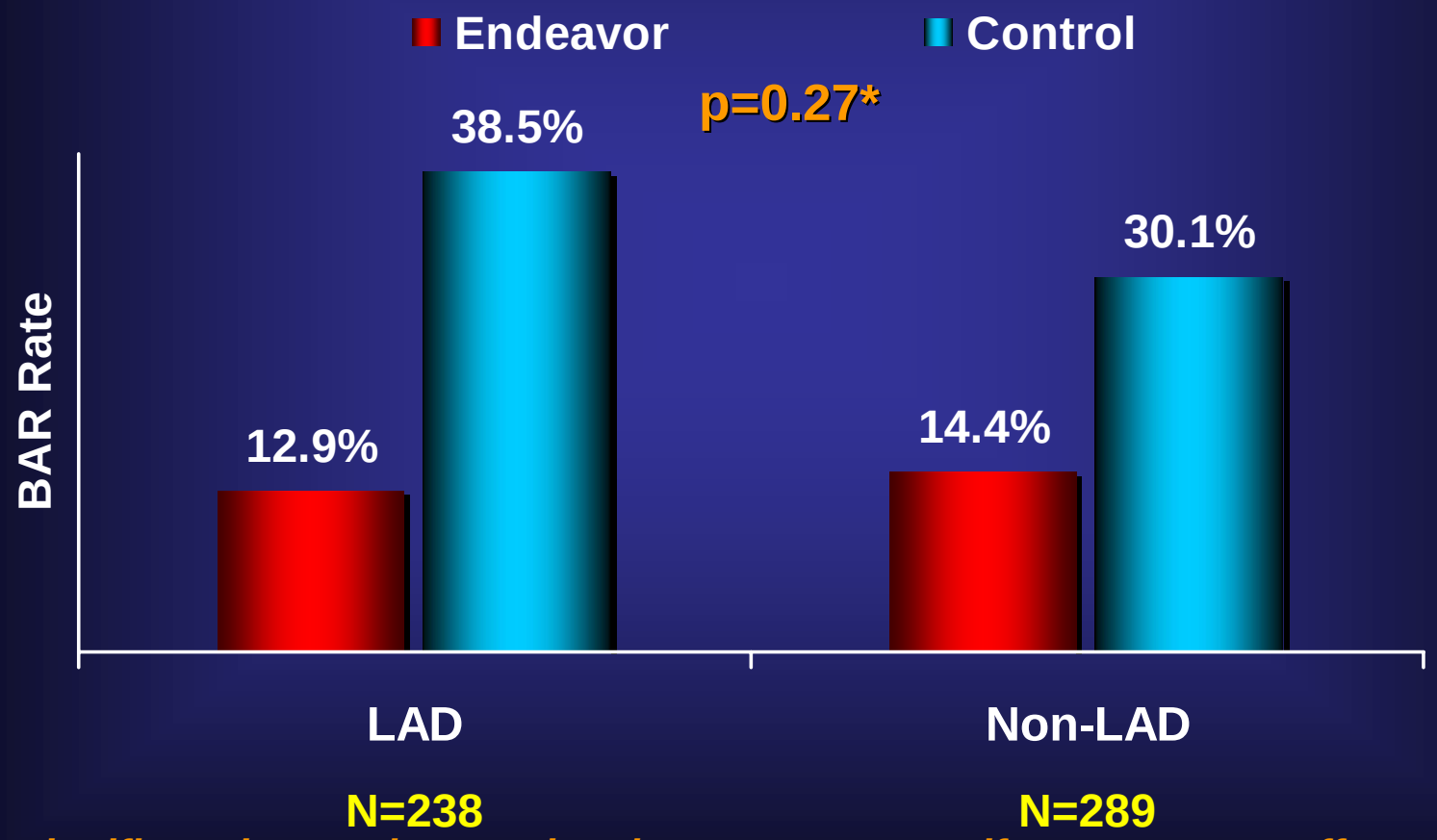
Binary Angiographic Restenosis

LAD Subset Analysis

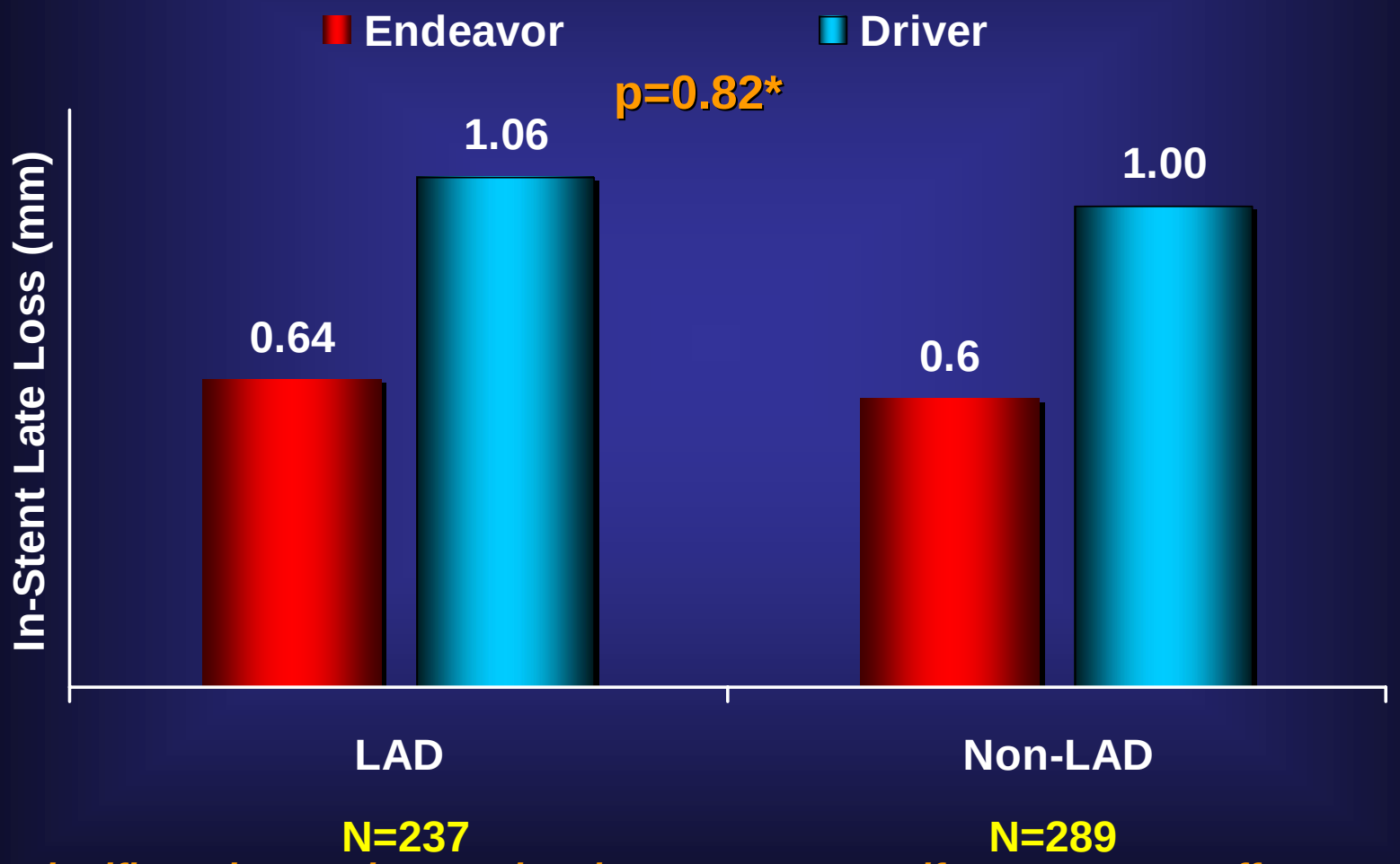


** Non-significant interaction p-value demonstrates a uniform treatment effect by LAD vs. non LAD lesion location*

Endeavor II

In-Stent Late Loss

LAD Subset Analysis



** Non-significant interaction p-value demonstrates a uniform treatment effect by LAD vs. non LAD lesion location*

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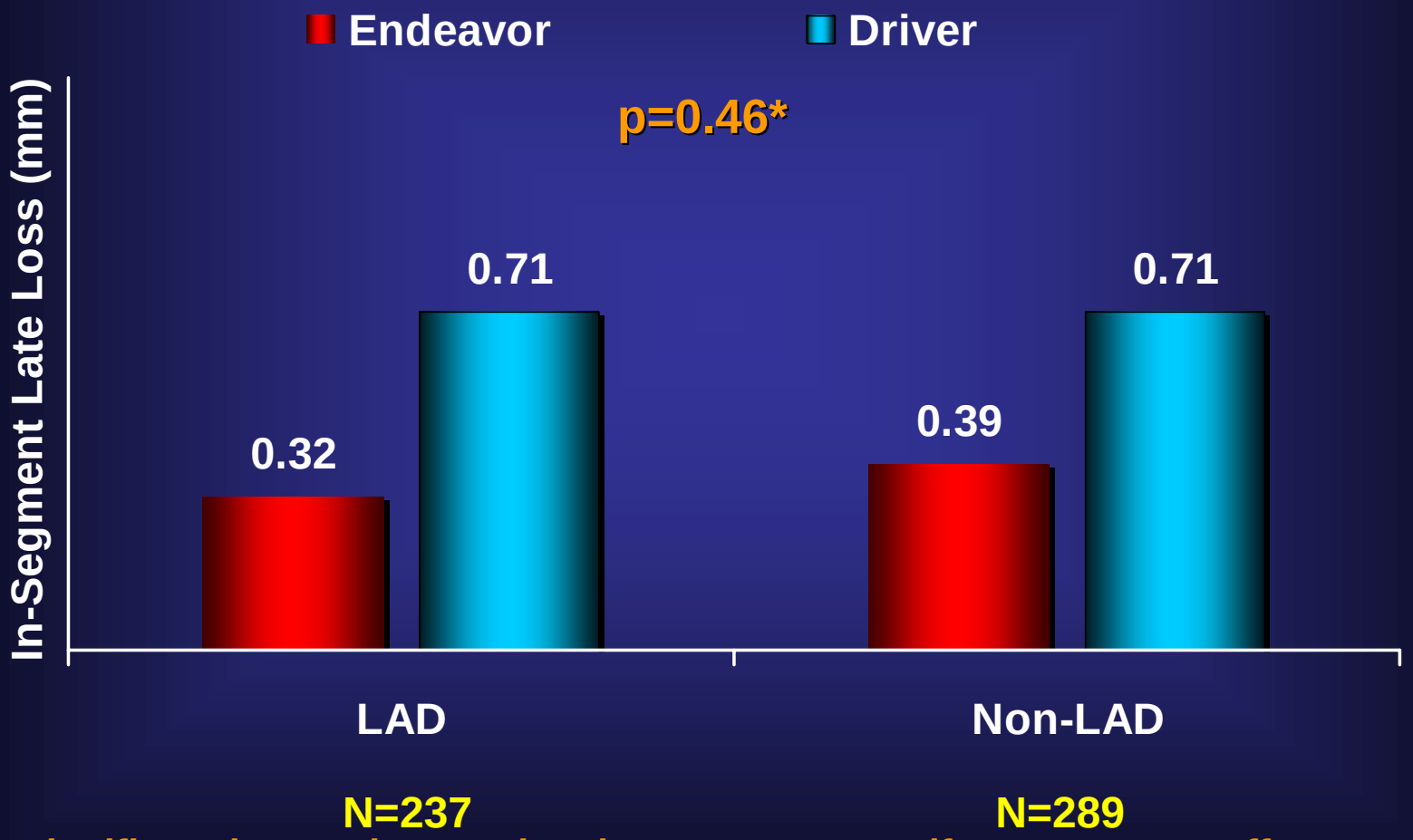
In-Segment Late Loss

LAD Subset Analysis



** Non-significant interaction p-value demonstrates a uniform treatment effect by LAD vs. non LAD lesion location*

Endeavor II

Two-way Models of LAD Location and Restenosis

Outcome Variable	TLR		In-segment BAR		In-stent late loss (mm)		In-segment late loss (mm)	
	OR	P-value	OR	P-value	β Coeff	P-value	β Coeff	P-value
LAD Location	1.49	0.06	1.23	0.33	0.05	0.30	-0.03	0.35
Treatment Assignment	0.36	<0.001	0.30	<0.001	-0.41	<0.0001	-0.36	<0.0001
LAD Interaction (p-value)		0.047		0.36		0.82		0.46

RVD: Reference vessel diameter, TLR: target lesion revascularization, In-segment BAR: In-segment binary angiographic restenosis, OR: Odds Ratio.

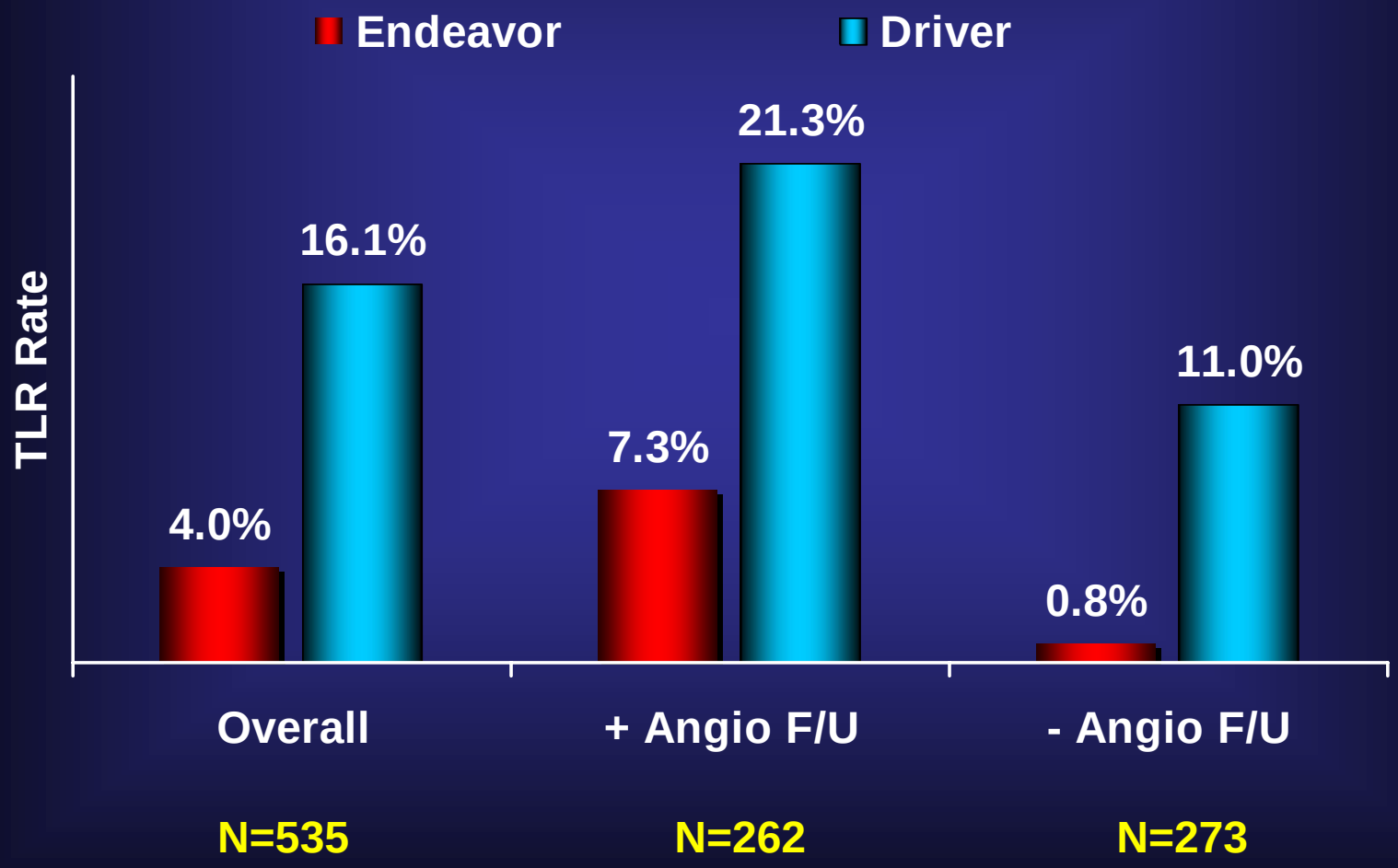
Borderline LAD and TLR interaction demonstrates a mild differential treatment effect for Endeavor and LAD

ACC Late Breaking Trials, 6 March 2005

Endeavor II

TLR by Angiographic Follow-up

LAD Subset Analysis



ACC Late Breaking Trials, 6 March 2005

Summary Statements

ENDEAVOR II is a 1200 patient, international, randomized, pivotal trial on the safety and efficacy of the Endeavor ABT578-eluting stent with high compliance and follow-up rates (> 97% clinical and > 88% angiographic follow-up)

The primary endpoint demonstrates a 47% reduction in Target Vessel Failure from 15.4% with the Driver stent to 8.1% with Endeavor. Treatment effect is achieved uniformly across the studied lesion subsets

These clinical results are obtained through an antiproliferative effect that reduces in-stent late loss from 1.02 mm with Driver to 0.62 mm with Endeavor. Stent thrombosis rates are low (0.5% for Endeavor) and there is no evidence for acquired late stent malapposition

Conclusions

This pivotal trial provides the evidence that the Endeavor drug-eluting stent is safe and substantially reduces clinical restenosis compared to bare-metal stent

Taken together with the ease of use of the Driver stent platform, the results of this trial establish the Endeavor stent as a valuable treatment option for patients undergoing angioplasty with drug-eluting stents