

Medtronic Vascular

Endeavor Safety Analysis

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ENDEAVOR I



Phase I FIM
36 month results

ENDEAVOR II



Double-blind Randomized Trial
24 month results

ENDEAVOR II CA Registry



Continued Access Safety
24 month results

ENDEAVOR III



Confirmatory Trial
vs. Cypher
12 month results

ENDEAVOR IV



Confirmatory Trial
vs. Taxus
30 day results

Endeavor Japan



Single Arm Trial
Enrollment completed

E-Five Registry



Real-World Performance and Safety
Evaluation
Enrollment completed

PROTECT



Head-to-Head Endeavor vs. Cypher
Safety Study
8,000 patient RCT

ENDEAVOR I
n=97/100 (97%)



Phase I FIM
36 month results

ENDEAVOR II
n=583/598 (97%)



Double-blind Randomized Trial
24 month results

ENDEAVOR II CA Registry
n=288/296 (97%)



Continued Access Safety
24 month results

ENDEAVOR III
n=320/323 (99%)



Confirmatory Trial
vs. Cypher
12 month results

ENDEAVOR IV
n=764/773 (99%)



Confirmatory Trial
vs. Taxus
30 day results

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Endeavor Safety Analysis

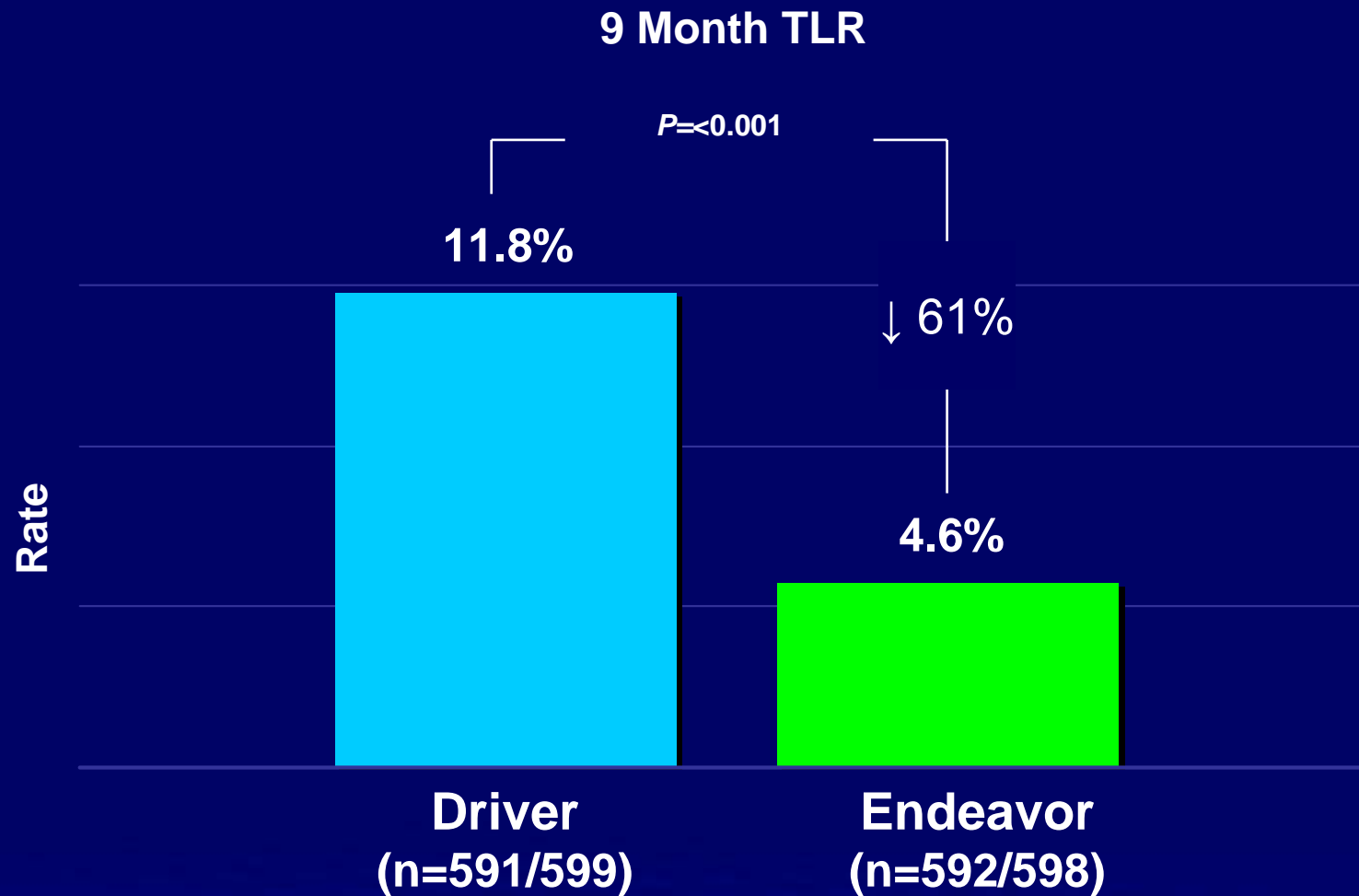
- The data presented yesterday for the available DES in the US indicated that these devices are important advancements:
 - by reducing the need for revascularization
 - without a statistical increase in the incidence of MI and death
- Any increased incidence of LST appeared to be offset by a reduction in downstream revascularization events prevented by DES

Endeavor Safety Analysis

- An ideal DES would:
 - 1) Reduce the incidence of revascularization and its downstream events **and**
 - 2) Provide equivalent or better safety results compared with BMS
- Such an ideal stent would be associated with a lower overall death and MI rate compared with BMS
- Approved and new candidate DES should not be viewed as a “class”

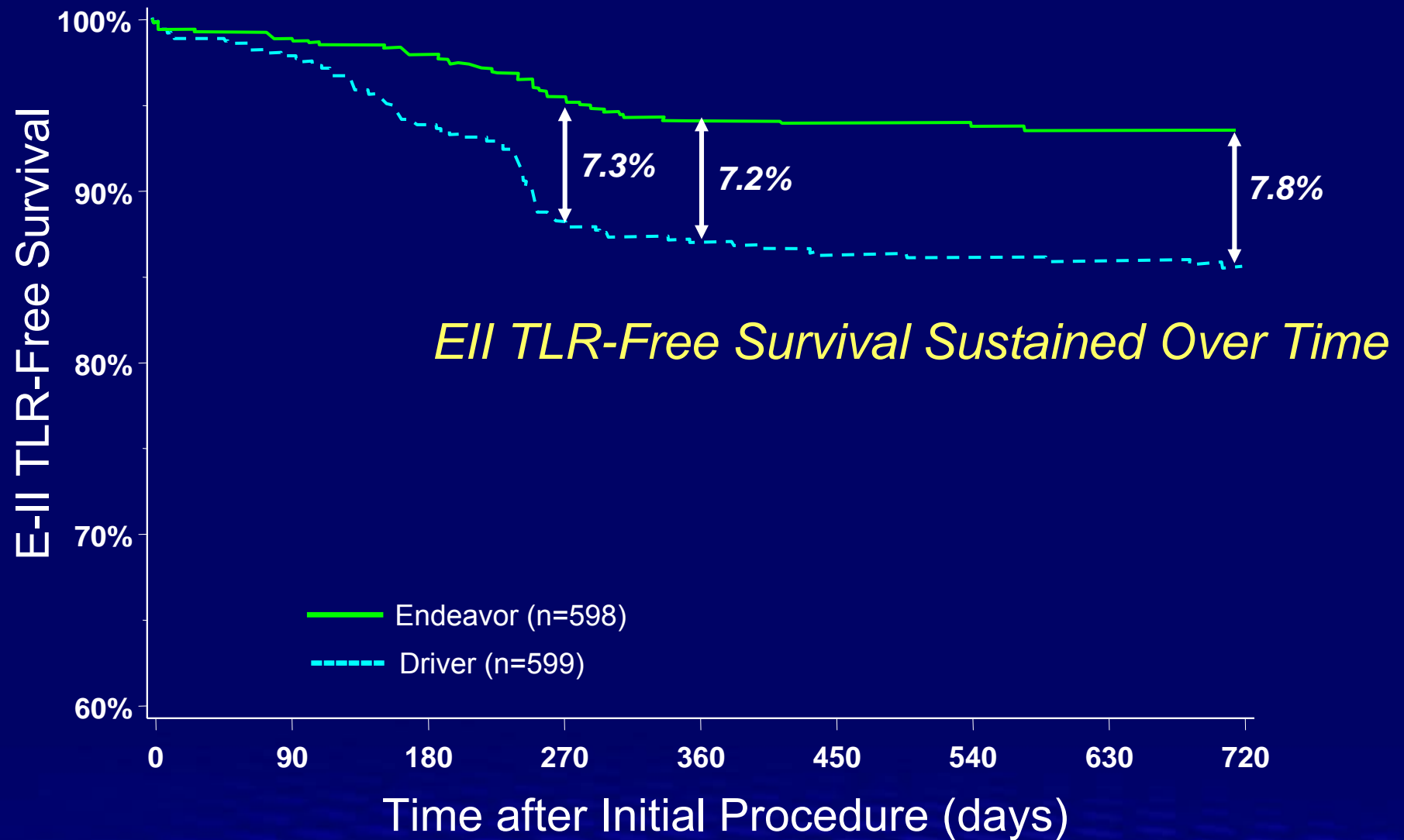
ENDEAVOR II

Target Lesion Revascularization



ENDEAVOR II

TLR Free Survival K-M to 2 years



Pre-specified HCRI CEC Stent Thrombosis Definition

- CEC process for adjudication of **Definite/Confirmed ST** has been the same for all major trials of DES.
 - Unexplained deaths within 30 days
 - Acute myocardial ischemia (ECG major ST abnormality or any biomarker elevation) **AND**
 - Angiographic or autopsy evidence of stent occlusion or thrombus. **AND**
 - Absence of intervening TLR
- **Possible/Presumed ST**
 - MI in target vessel territory without angiographic evidence of thrombus or other culprit

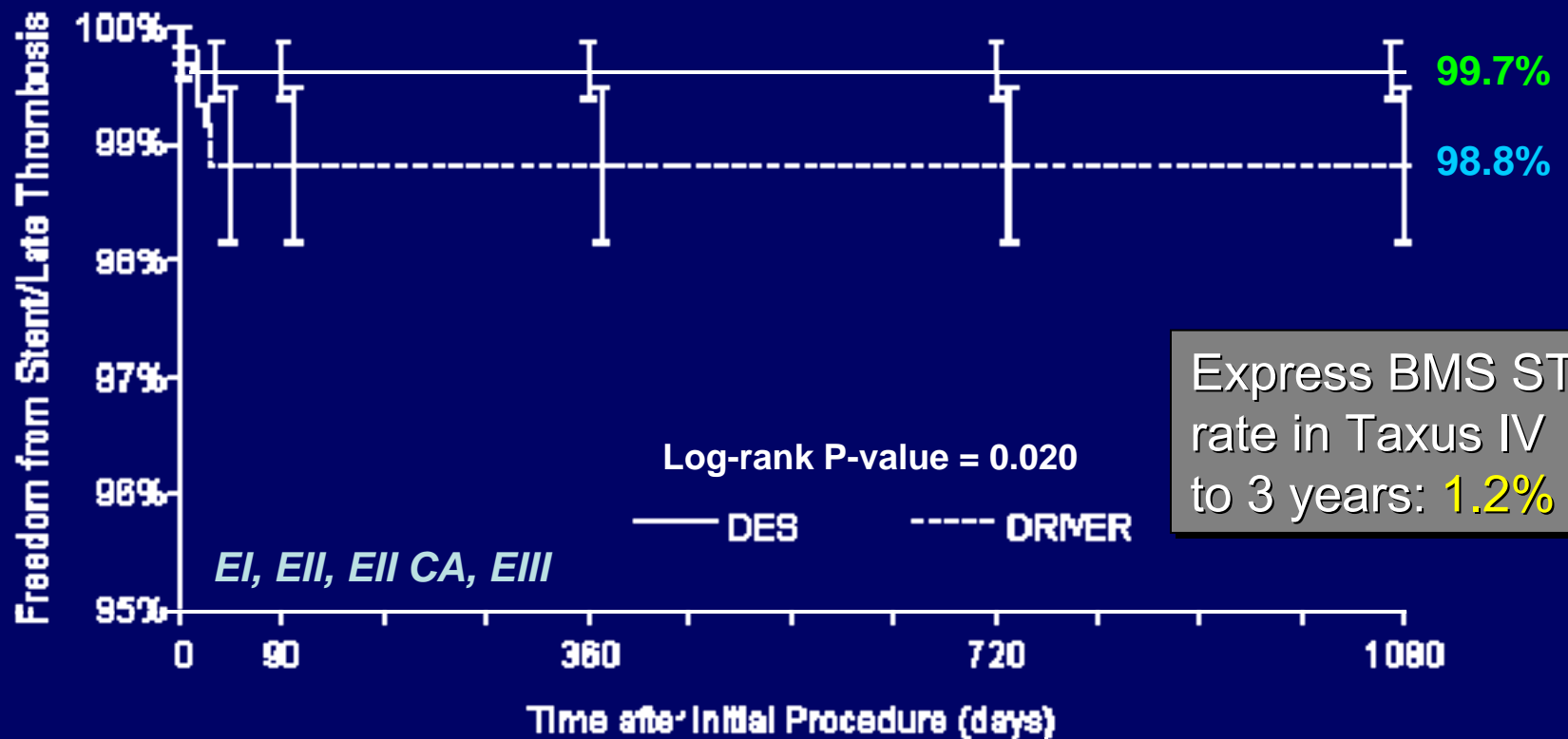
Endeavor safety analysis

*Rate of Stent Thrombosis According to the Prospective HCRI
CEC Definition by study*

	Early (≤ 30 days)	LaST ($>30 - 365$ d)	V LaST (>365 d)
ENDEAVOR I n=97/100 to 3 yrs	1 (1%)	0	0
ENDEAVOR II n=583/598 to 2 yrs	3 (0.5%)	0	0
ENDEAVOR IICA n=288/296 to 2 yrs	0	0	0
ENDEAVOR III n=320/323 to 1 yr	0	0	N/A

Endeavor Safety Compared to Driver

Pre-specified HCRI CEC Defined Stent Thrombosis 3 yr K-M



Days	30	90	360	720	1080
Endeavor	1315	1309	1303	1206	690
# Events	4	0	0	0	0
Driver	596	587	585	568	382
# Events	7	0	0	0	0

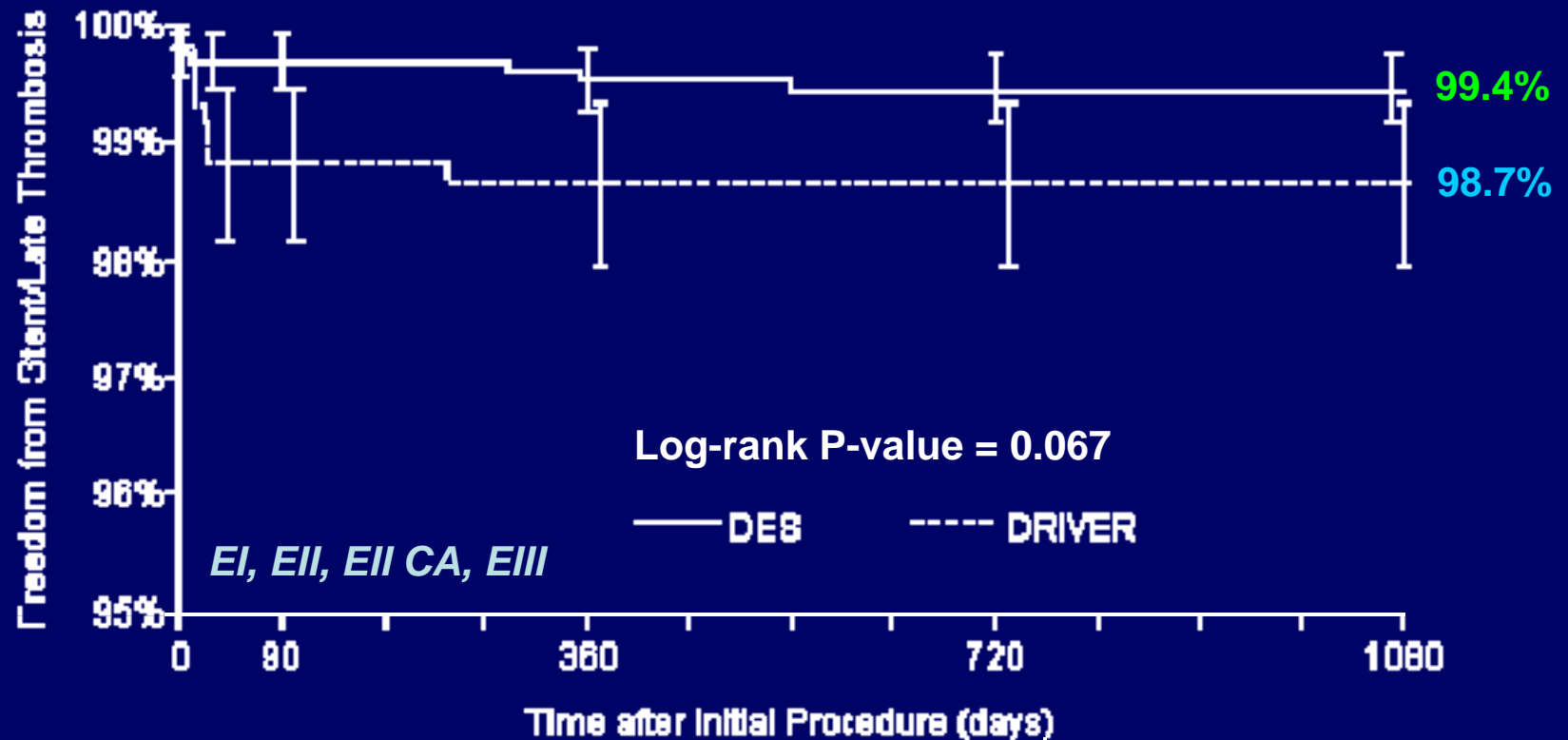
Endeavor Safety Compared to Driver

ARC Definition: Cumulative Definite/Probable

Thrombosis	Endeavor (n=1,316)	Driver (n=596)
Early ST	4 (0.3%)	7 (1.2%)
Definite	4	7
Probable	0	0
Late ST	2 (0.5%)	1 (0.2%)
Definite	2	1
Probable	0	0
Very Late ST	1 (0.1%)	0 (0.0%)
Definite	0	0
Probable	1	0
Totals	7 (0.5%)	8 (2.3%)

Stent Thrombosis Endeavor vs Driver

ARC Definition: Definite and Probable 3 yr K-M



Days	30	90	360	720	1080
Endeavor	1316	1309	1303	1159	690
# Events	4	0	2	1	0
Driver	596	587	585	567	382
# Events	7	0	1	0	0

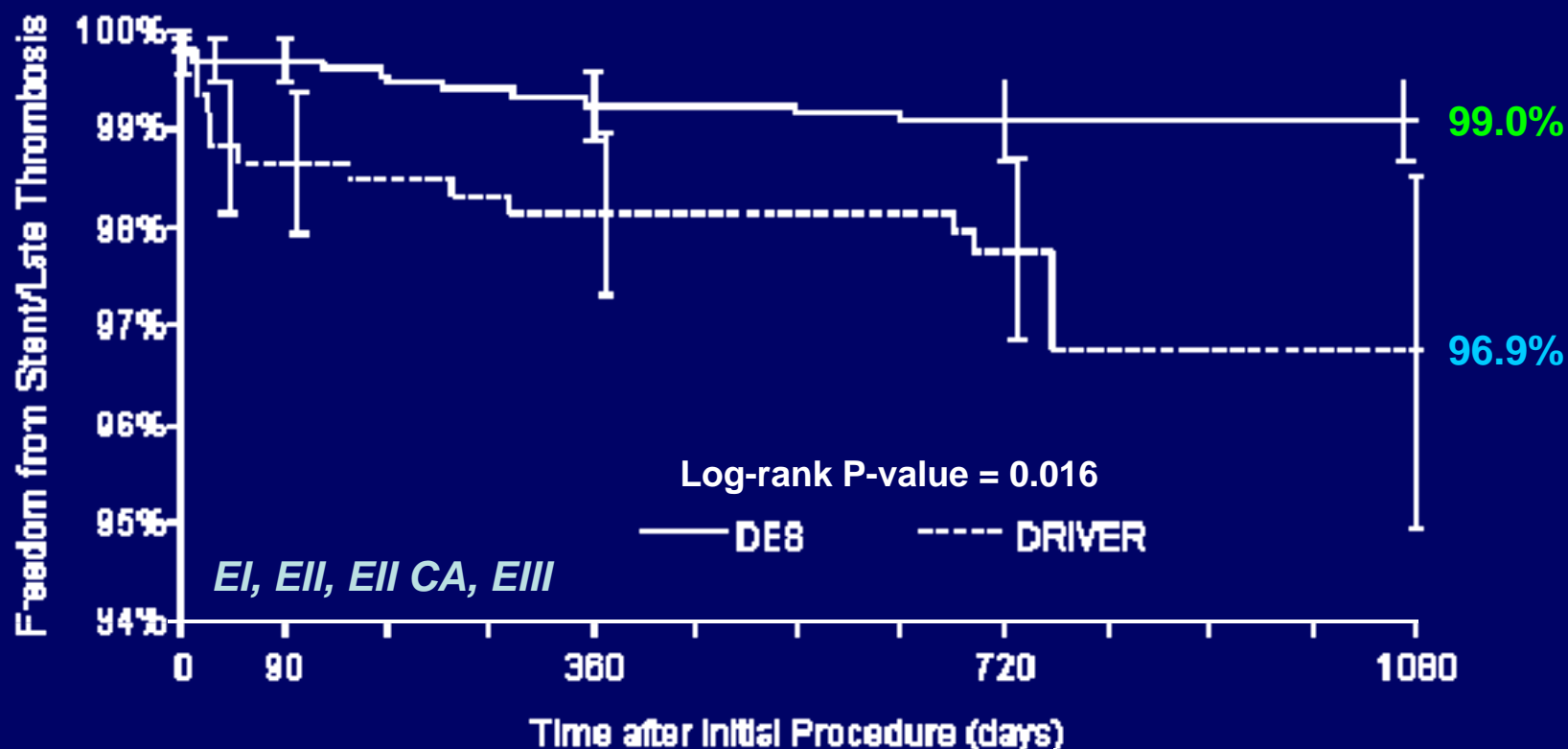
Endeavor Safety Compared to Driver

ARC Definition: Cumulative Definite, Probable, **Possible**

Thrombosis	Endeavor (n=1,316)	Driver (n=596)
Early (Any)	4 (0.3%)	7 (1.2%)
Definite	4	7
Probable	0	0
Late (Any)	6 (0.5%)	4 (0.7%)
Definite	2	1
Probable	0	0
Possible	4	3
Very Late (Any)	2 (0.2%)	3 (0.6%)
Definite	0	0
Probable	1	0
Possible	1	3
Totals	12 (1.0%)	14 (3.3%)

Stent Thrombosis Endeavor vs Driver

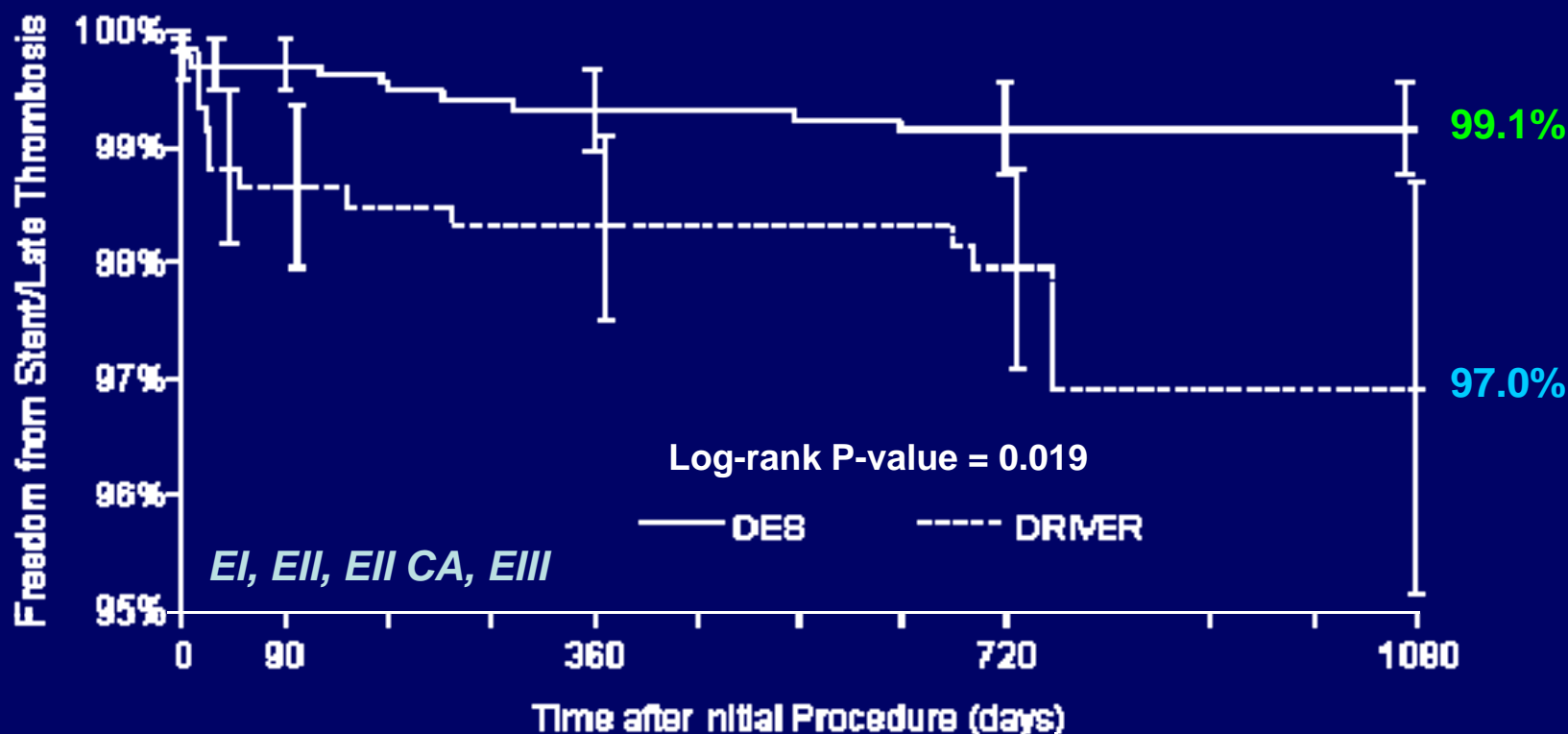
ARC Definition: Cumulative Definite, Probable, Possible



Days	30	90	360	720	1080
Endeavor	1316	1309	1303	1159	690
# Events	4	0	6	2	0
Driver	596	587	585	567	382
# Events	7	1	3	2	1

Stent Thrombosis Endeavor vs Driver

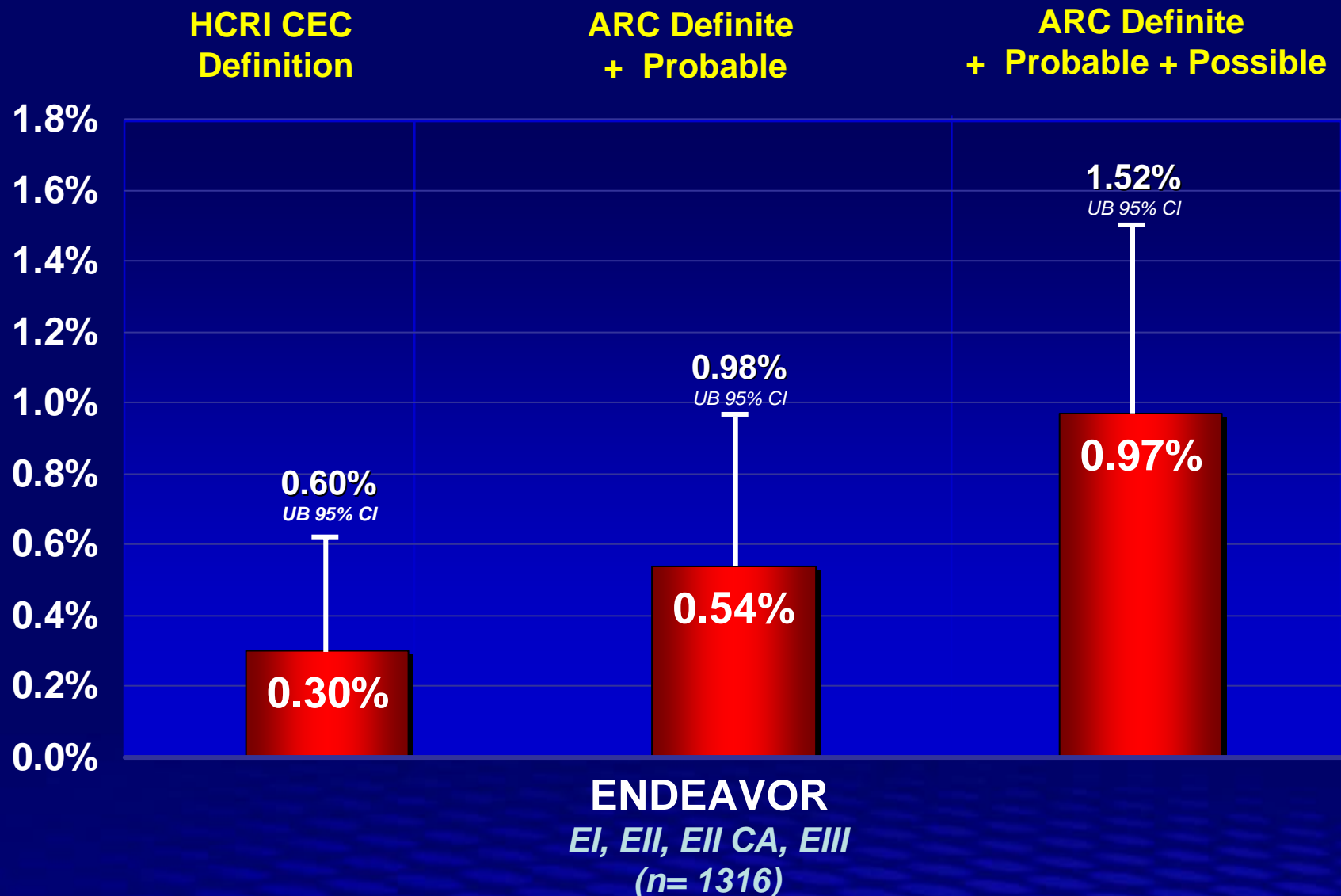
ARC Possible/Probable/Definite *Censoring TLR*



Days	30	90	360	720	1080
Endeavor	1316	1309	1303	1159	690
# Events	4	0	5	2	0
Driver	596	587	585	567	382
# Events	7	1	2	2	1

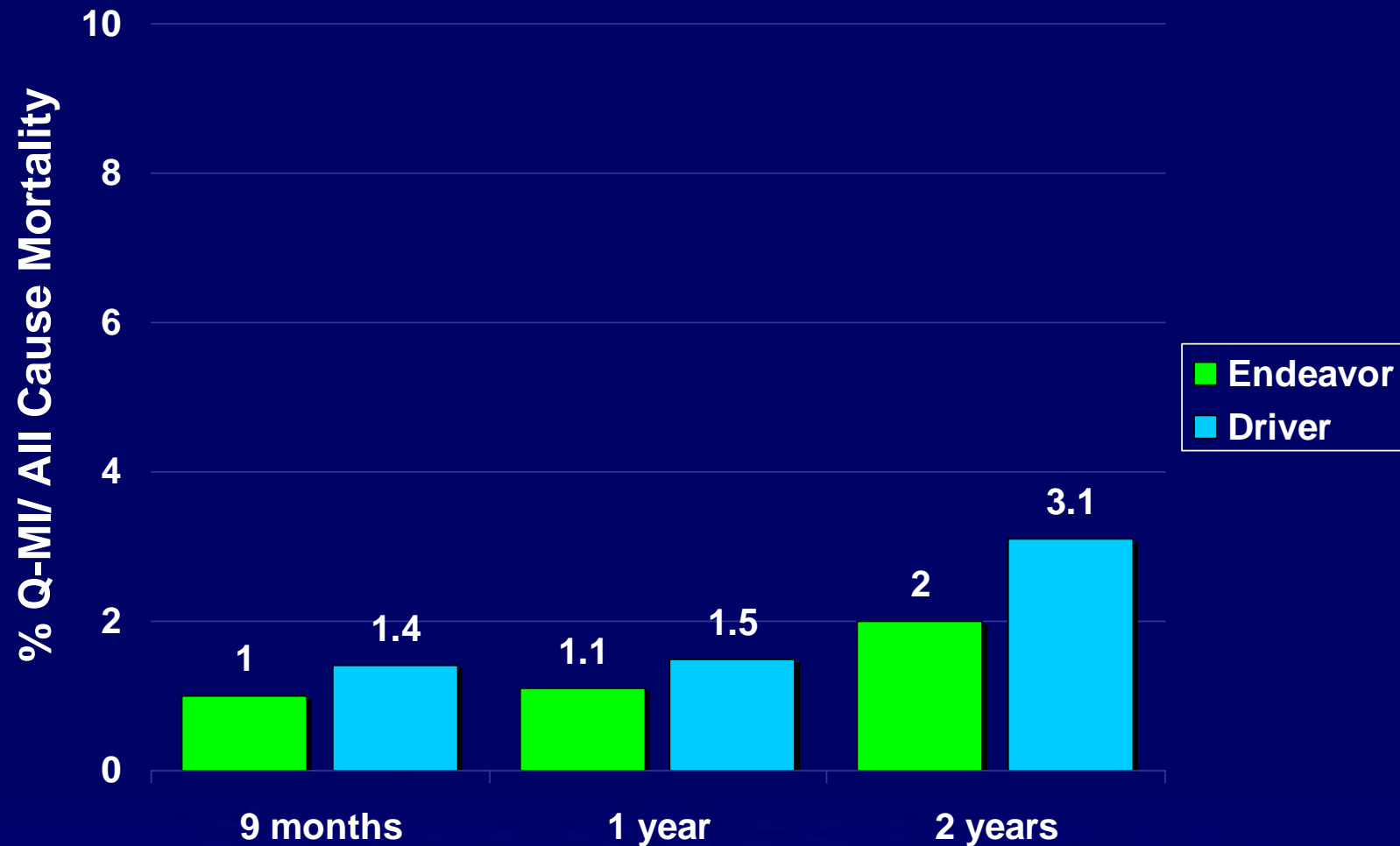
Endeavor Stent Thrombosis Rate :

HCRI CEC and ARC Definitions 3yr K-M estimate



Composite of QWMI/All Cause Mortality

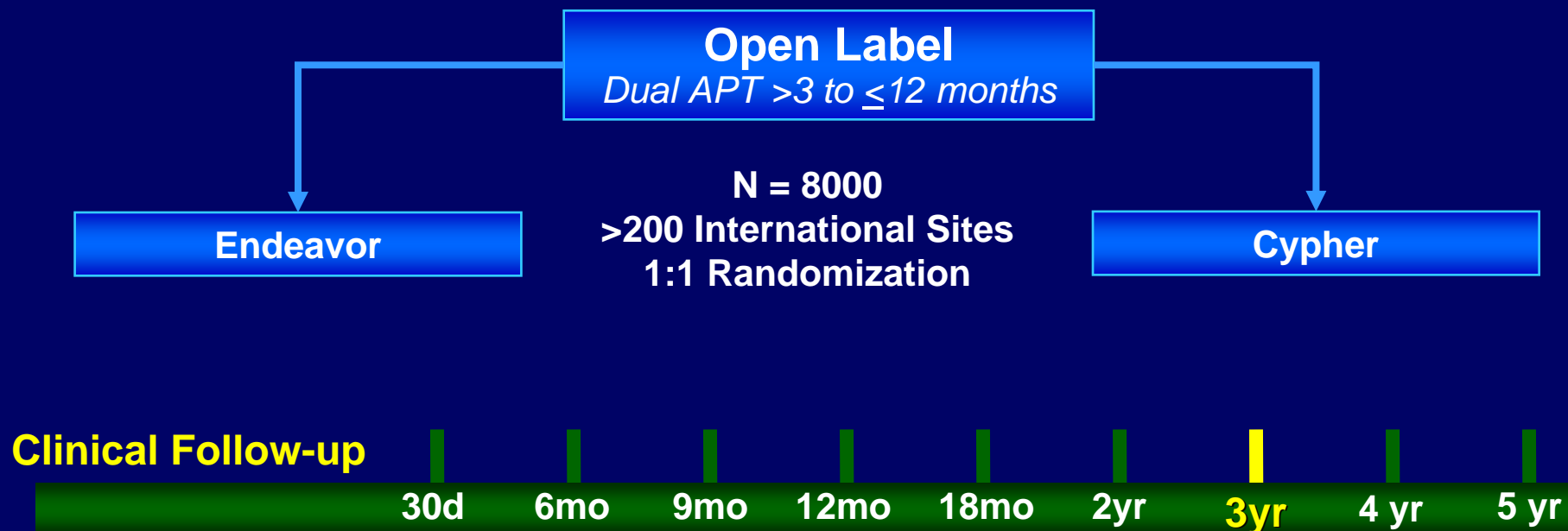
EI, EII, EII CA, EIII



Endeavor data: EI, EII, EII CA, EIII
Driver data: EII

Studying Expanded Use and Stent Thrombosis

PROTECT Clinical Trial Design



Primary Endpoint: Definite or Probable Stent Thrombosis to 3 years

Secondary Endpoints: Death/NF MI, Cardiac death/NF MI, TVR, TLR

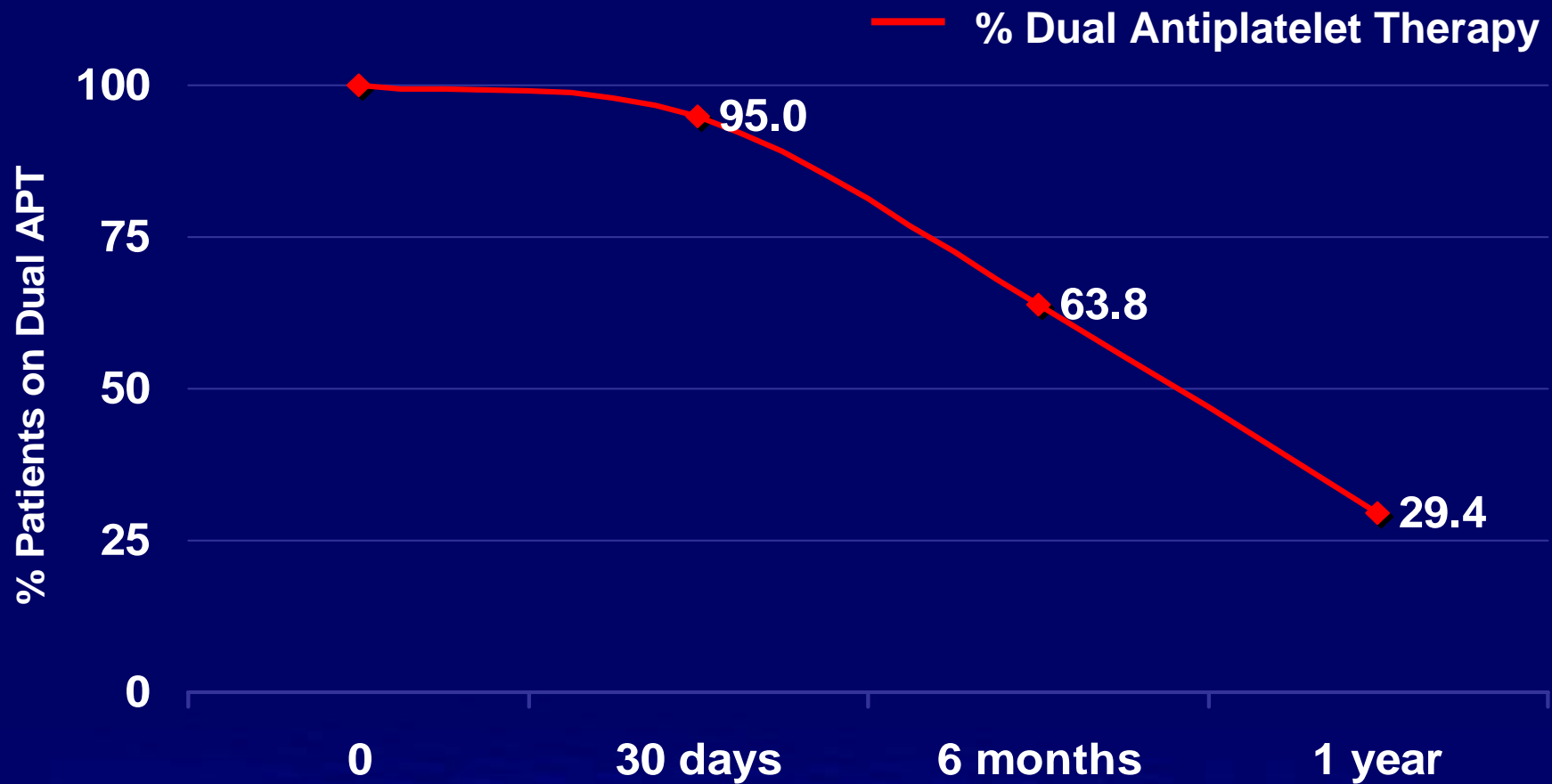
Co-PI's: W. Wijns (Belgium), P. Serruys (Netherlands),
G. Steg (France), E. Camezind (Switzerland), B. O'Neill (USA)

Summary

- **DES are not a class**
- **Available Endeavor data have demonstrated prevention of restenosis without an increased safety risk under ARC definitions**
- **Medtronic is committed to ongoing follow-up and new post-market studies**

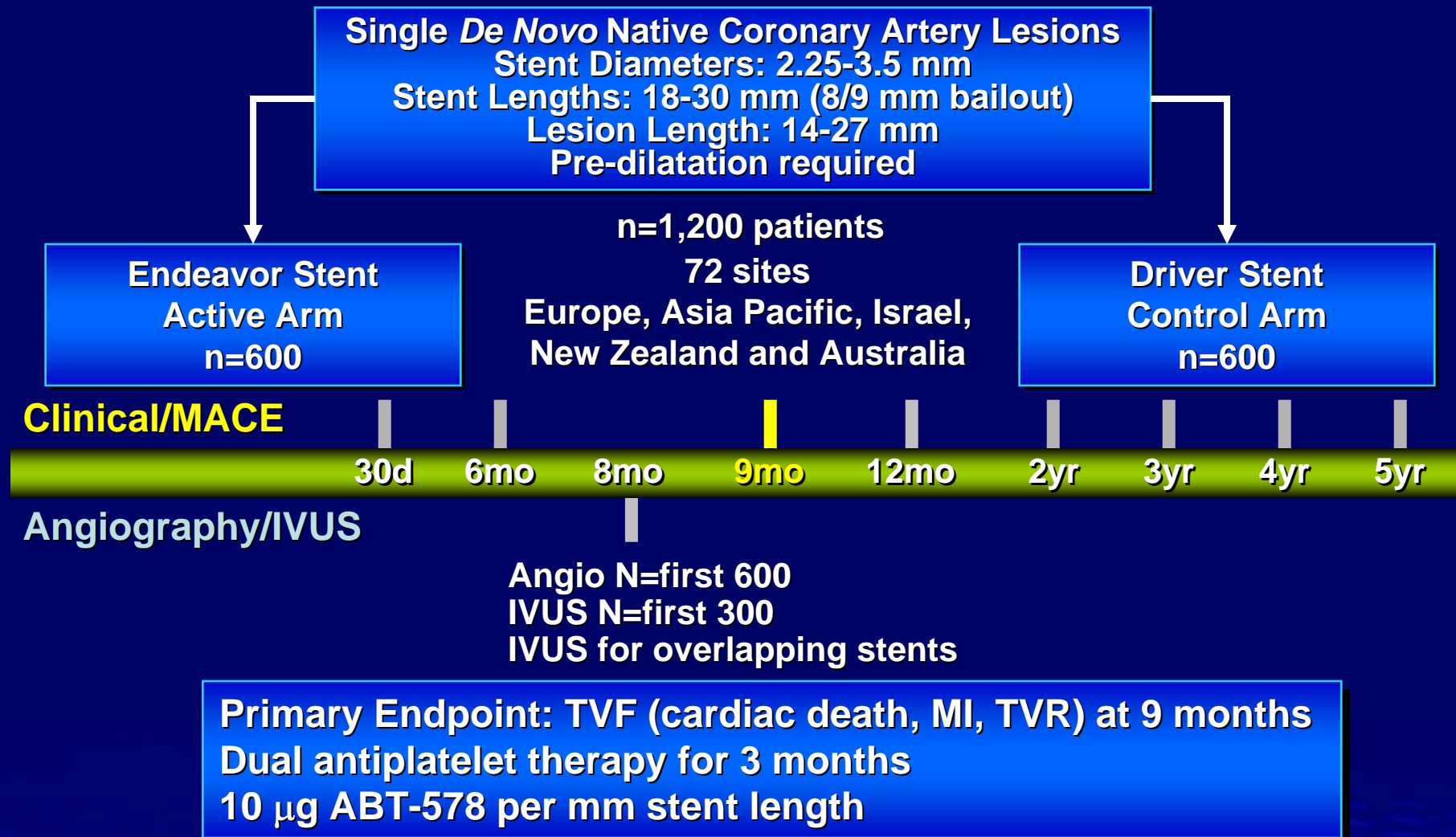
ENDEAVOR II

Adherence to Antiplatelet Therapy to 1 Year



ENDEAVOR II

Randomized, Double-Blind Trial Design



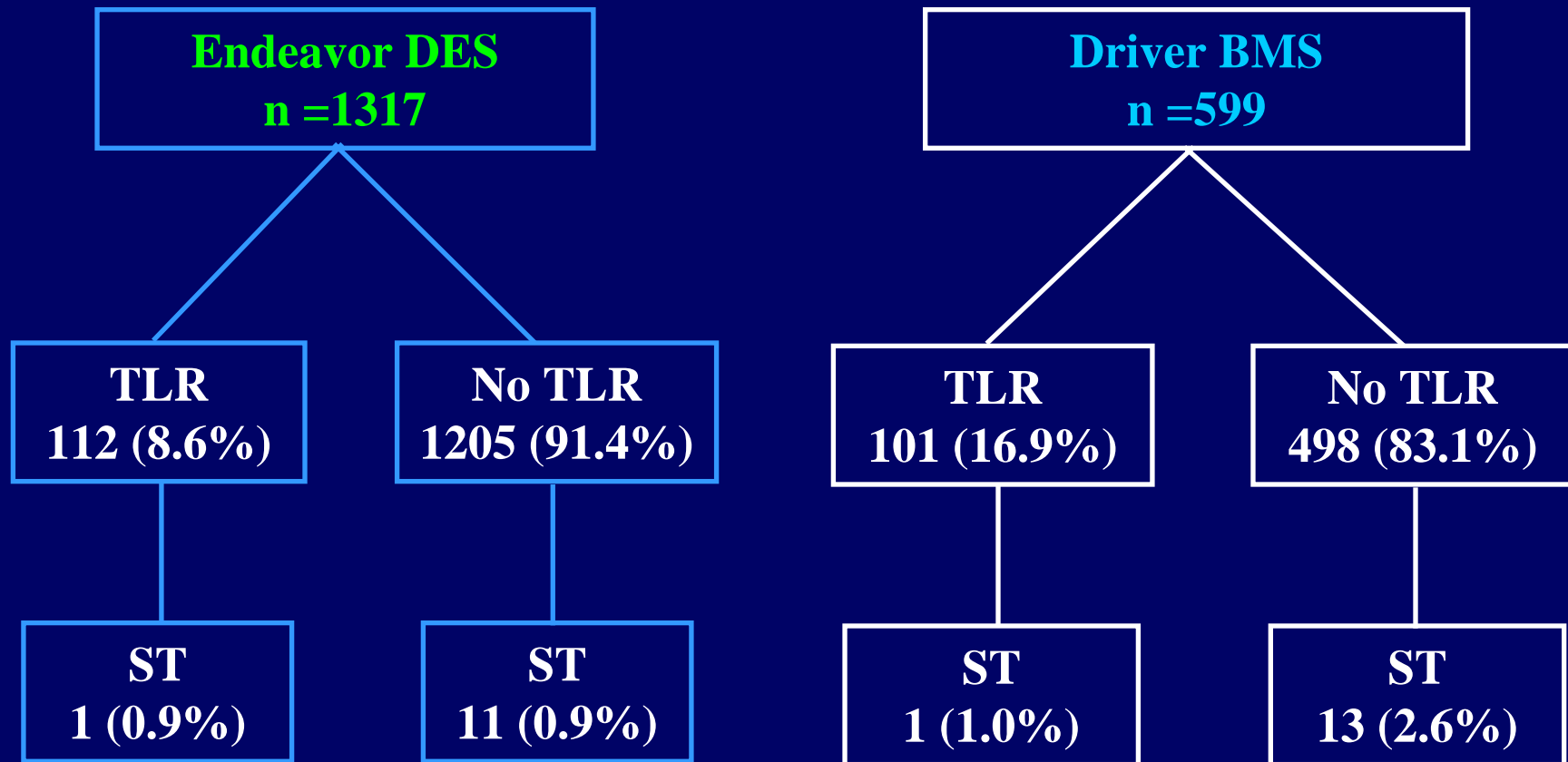
ENDEAVOR II

Patient 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 (%)	18.2	22.2	ns
Unstable Angina (%)	30.3	30.3	ns
Recent MI (%)	16.1	14.4	ns
Hyperlipidemia (%)	80.5	76.9	ns
History of smoking (%)	35.3	35.2	ns

Stent Thrombosis Endeavor vs Driver

Prior TLR and Any Stent Thrombosis



TLR = TLR (clinically-driven or non-clinically driven) prior to ST

ENDEAVOR Clinical Program

Late Incomplete Apposition

8 Month Results	EI* n=86	EII n=114	EIICA n=48	EIII n=190	Combined n=438
Late Incomplete Apposition (%)	0	0	0	0.5 (1) [†]	0.2 (1)

*EI results at 12 months.

[†]Thrombus at baseline resolved during follow-up. No aneurismal remodeling.