

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

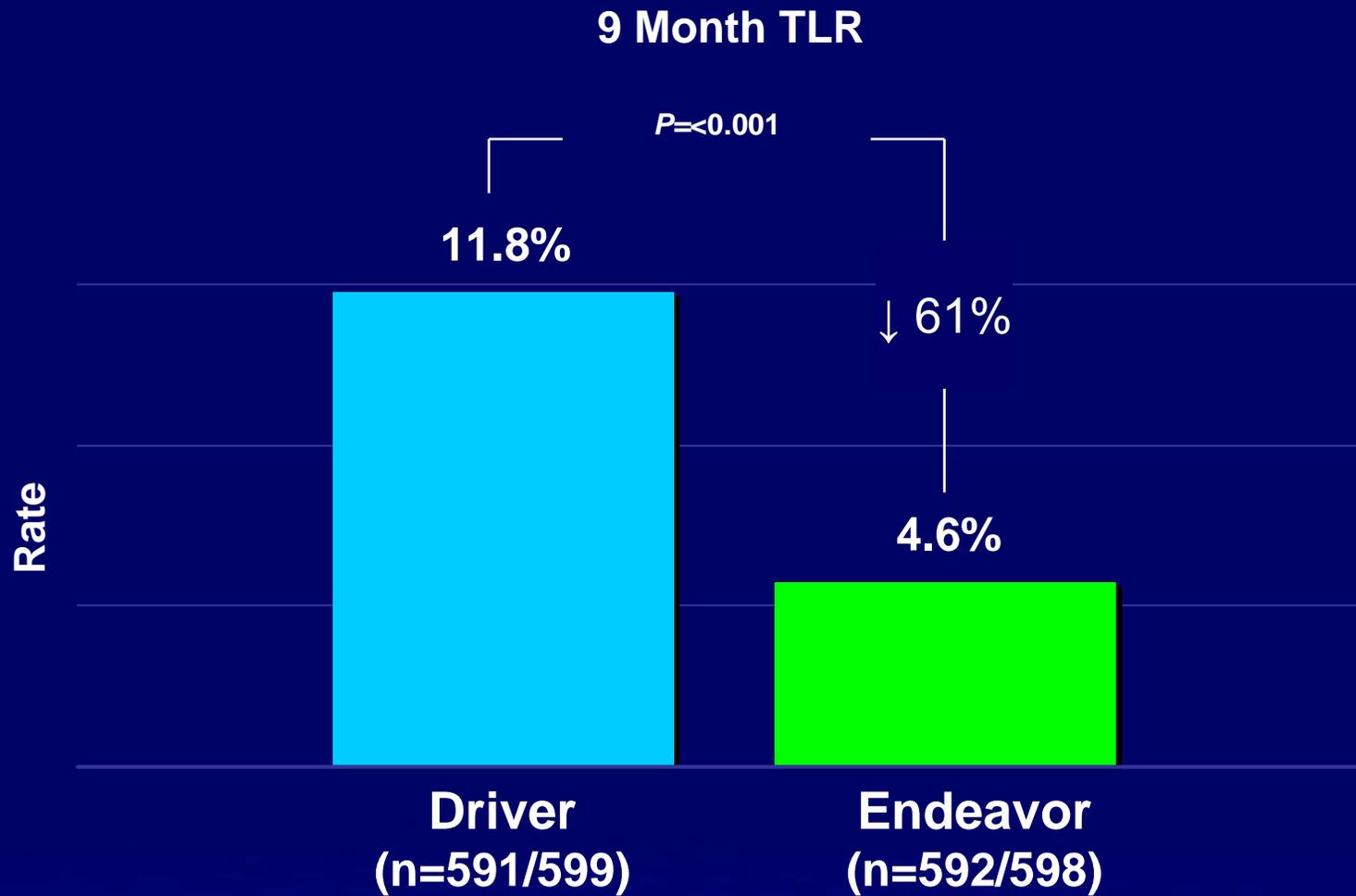
- The data presented yesterday for the available DES in the US indicated that these devices are important advancements:
 - by reducing the need for revascularization
 - without a statistical increase in the incidence of MI and death
- Any increased incidence of LST appeared to be offset by a reduction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

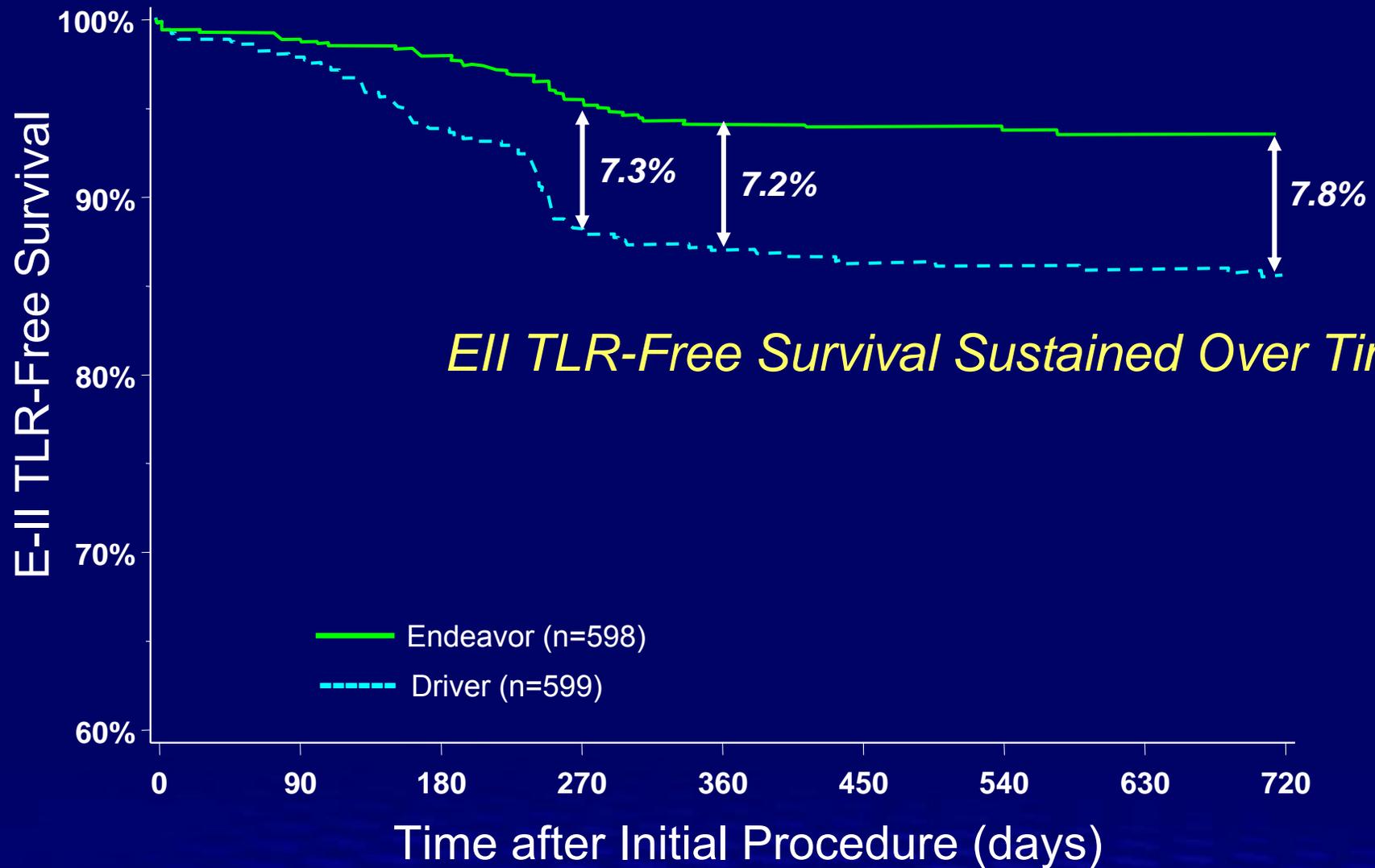
ENDEAVOR II

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

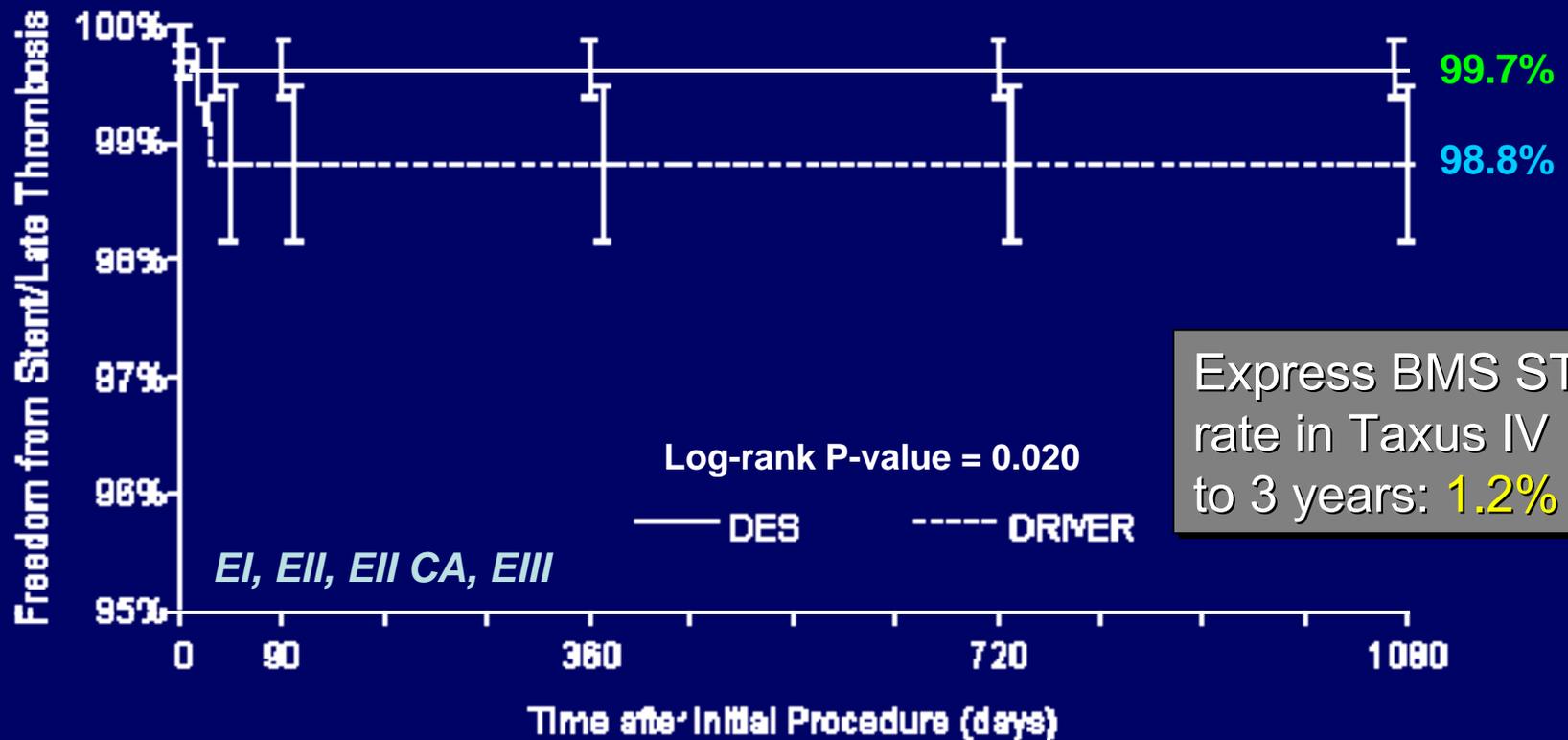
Endeavor safety analysis

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

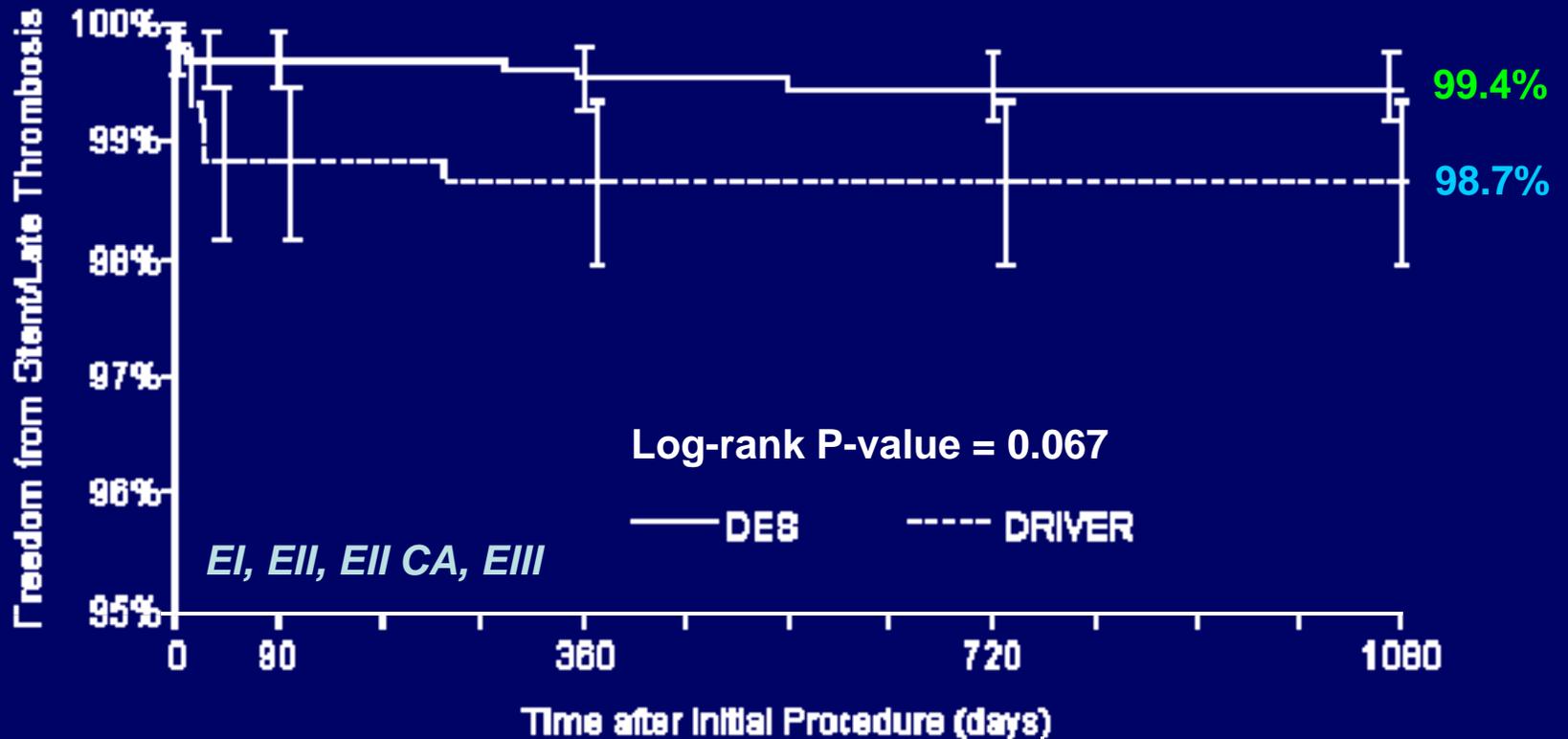
Endeavor Safety Compared to Driver

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

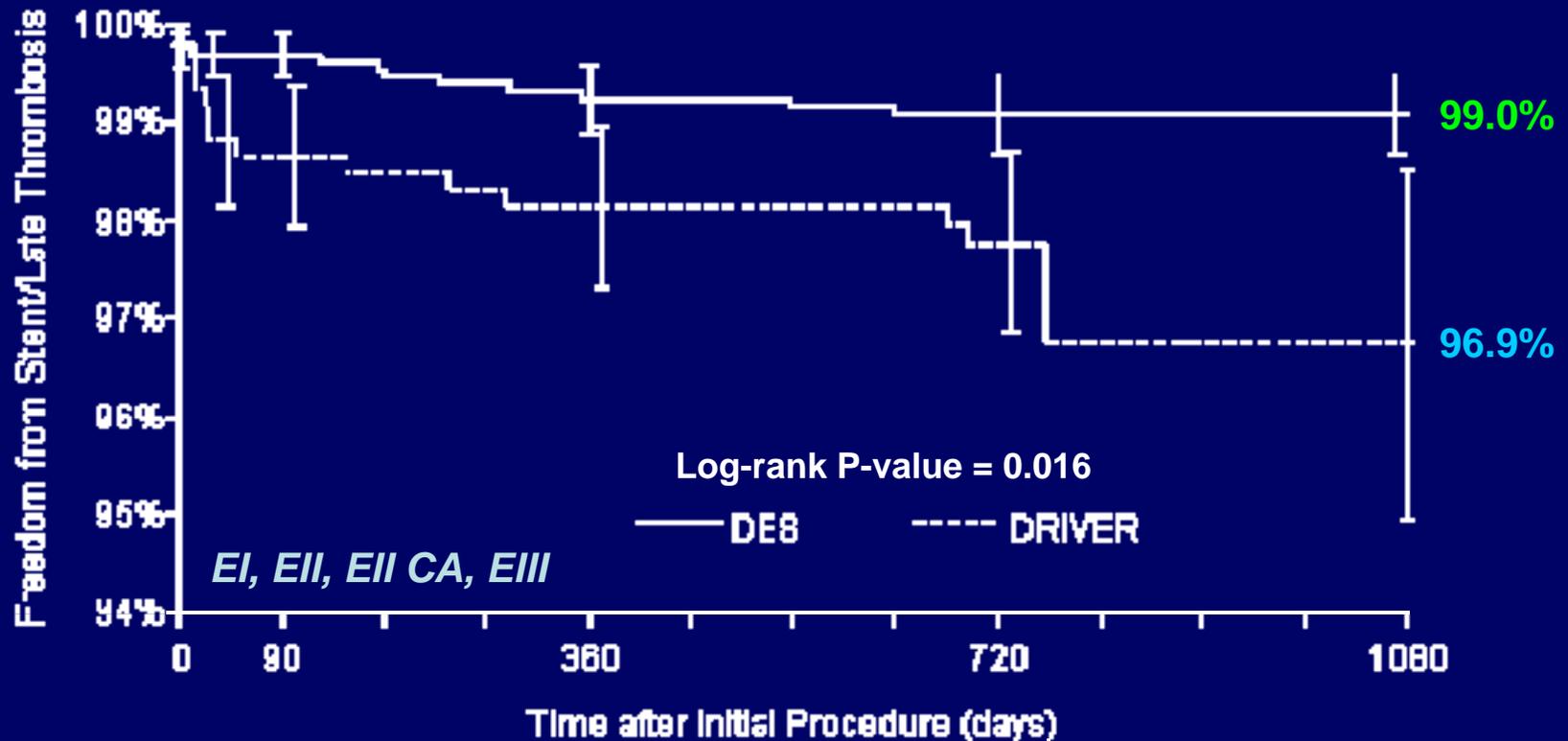
Endeavor Safety Compared to Driver

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

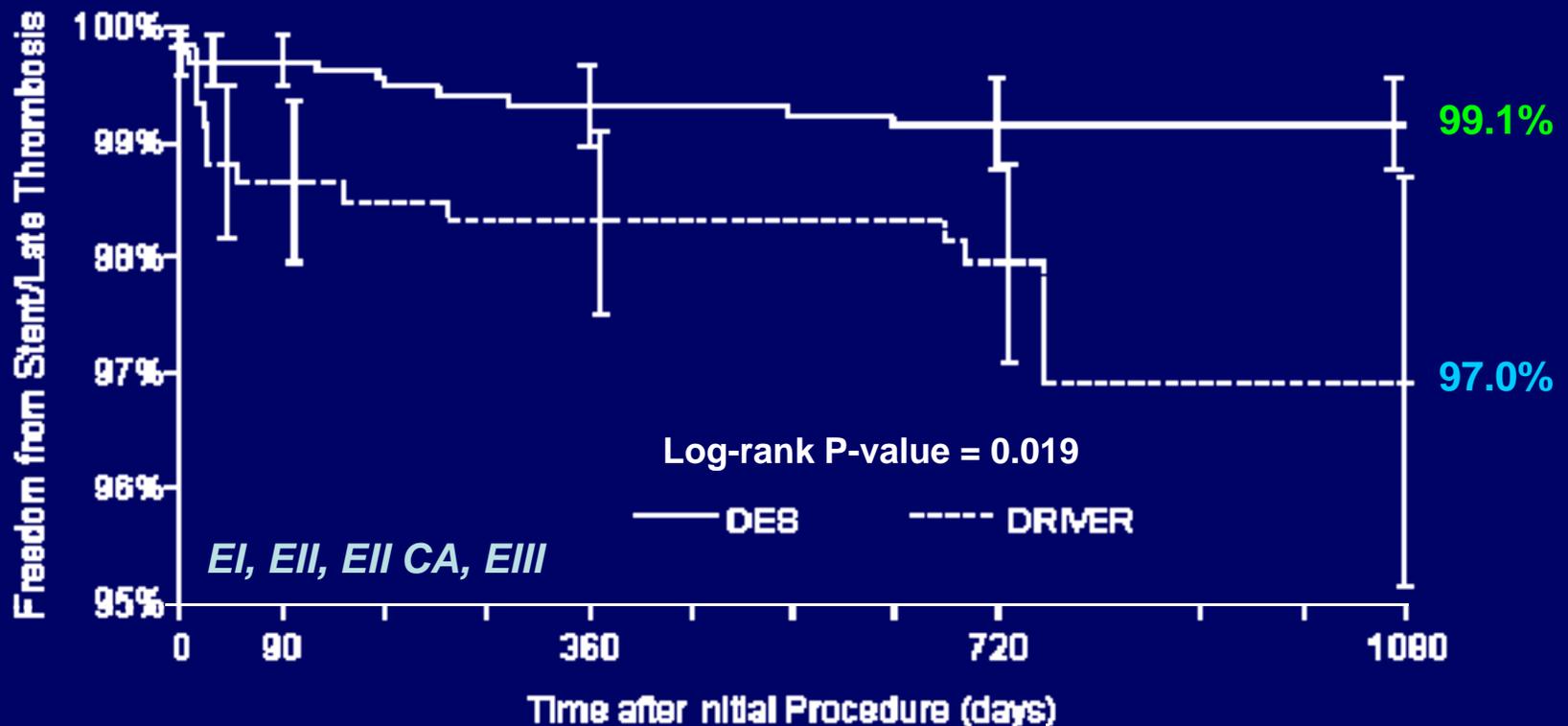
ARC Definition: Cumulative Definite, Probable, Possible



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

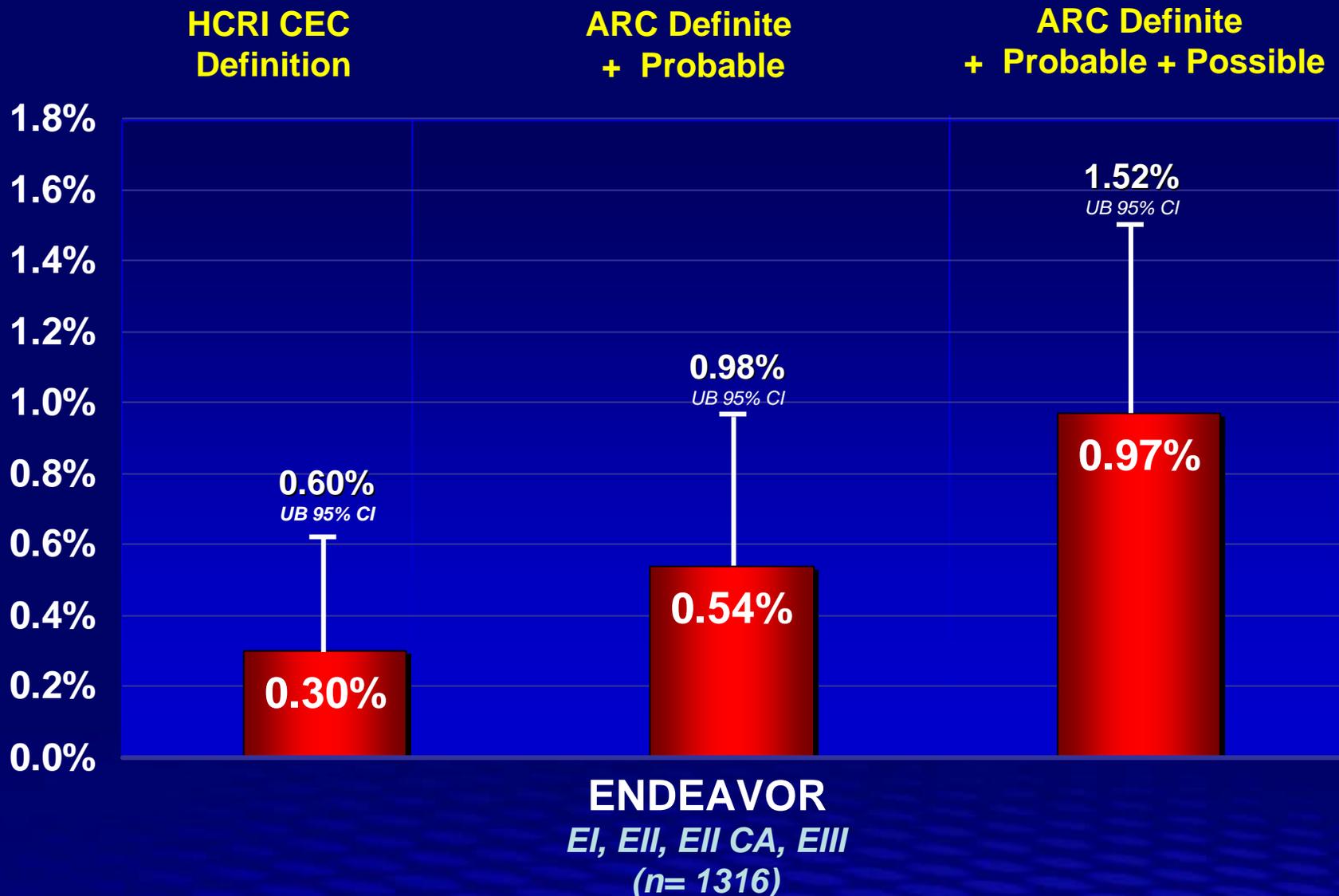
ARC Possible/Probable/Definite Censoring TLR



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

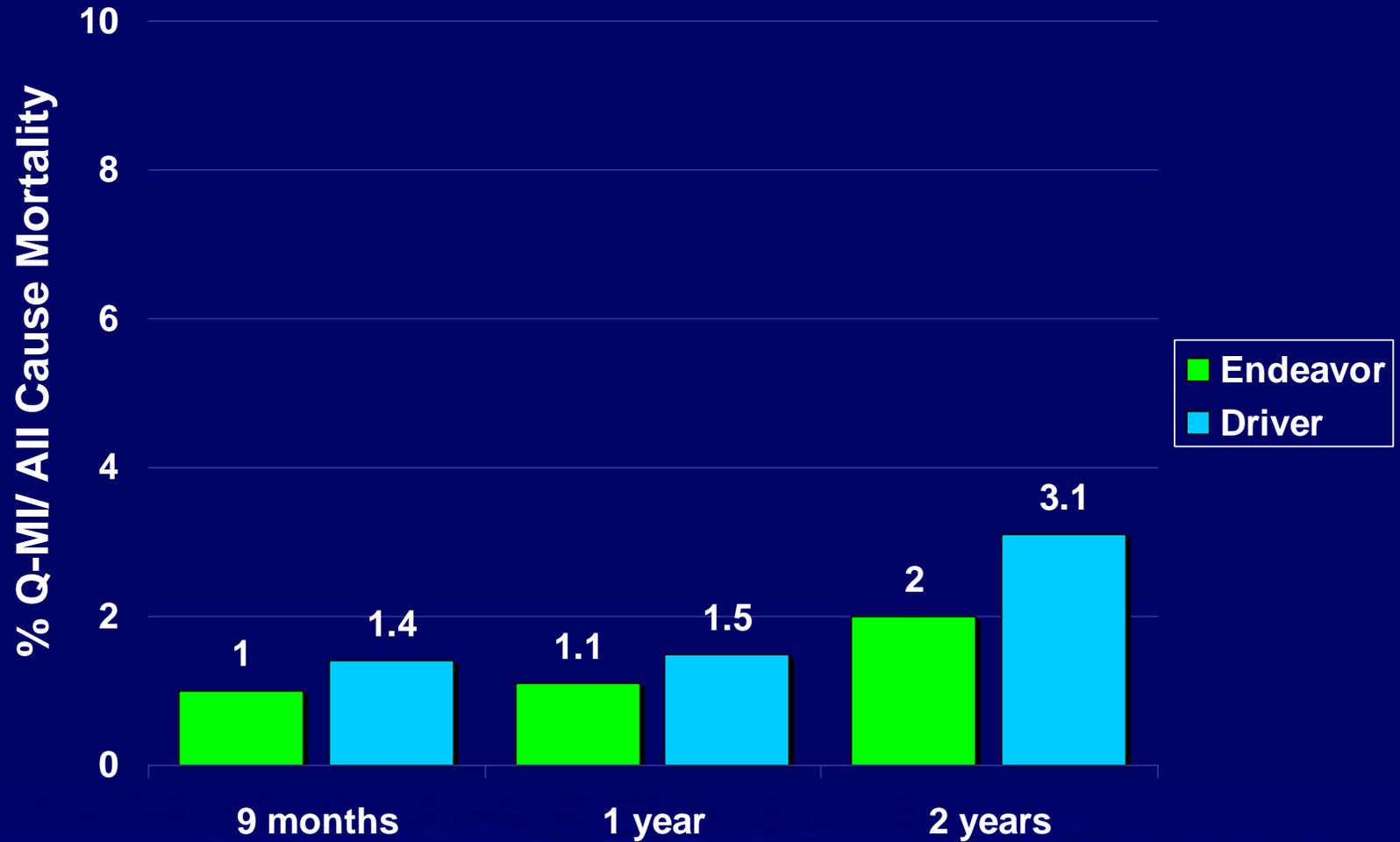
Endeavor Stent Thrombosis Rate :

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



Clinical Follow-up

30d

6mo

9mo

12mo

18mo

2yr

3yr

4 yr

5 yr

Primary Endpoint: Definite or Probable Stent Thrombosis to 3 years

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

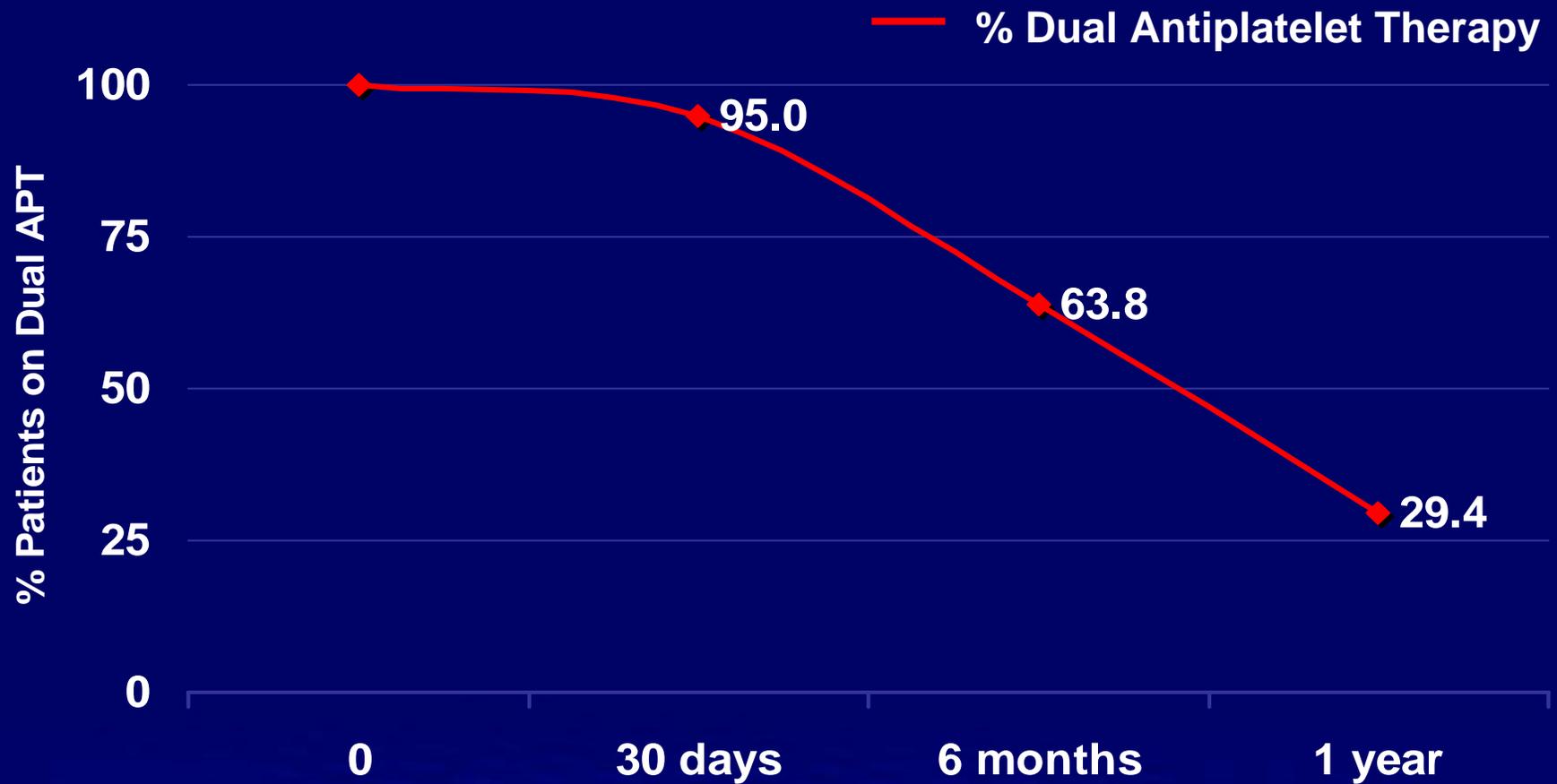
Co-PI's: W. Wijns (Belgium), P. Serruys (Netherlands),
G. Steg (France), E. Camezind (Switzerland), B. O'Neill (USA)

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**

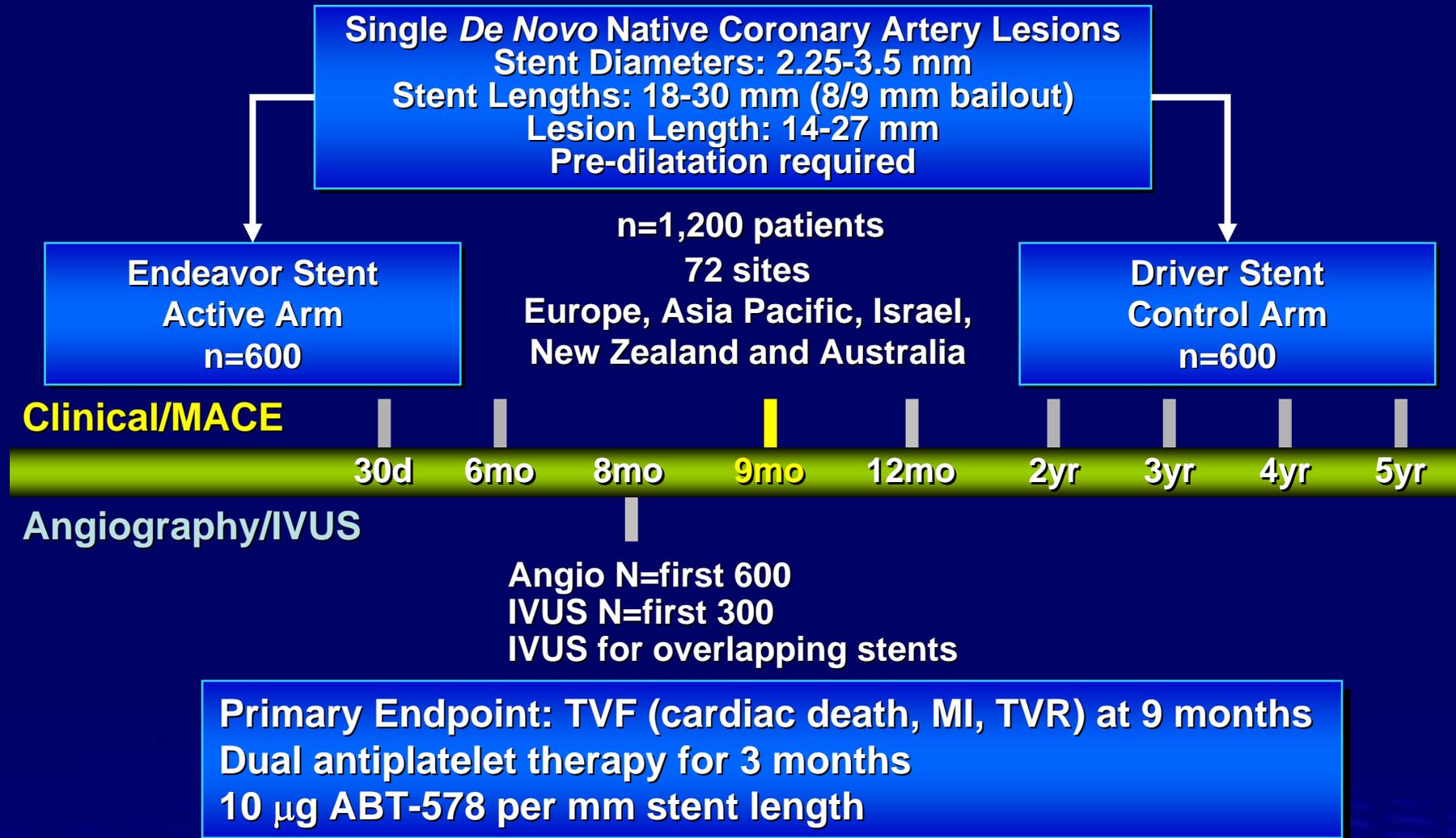
ENDEAVOR II

Adherence to Antiplatelet Therapy to 1 Year



ENDEAVOR II

Randomized, Double-Blind Trial Design



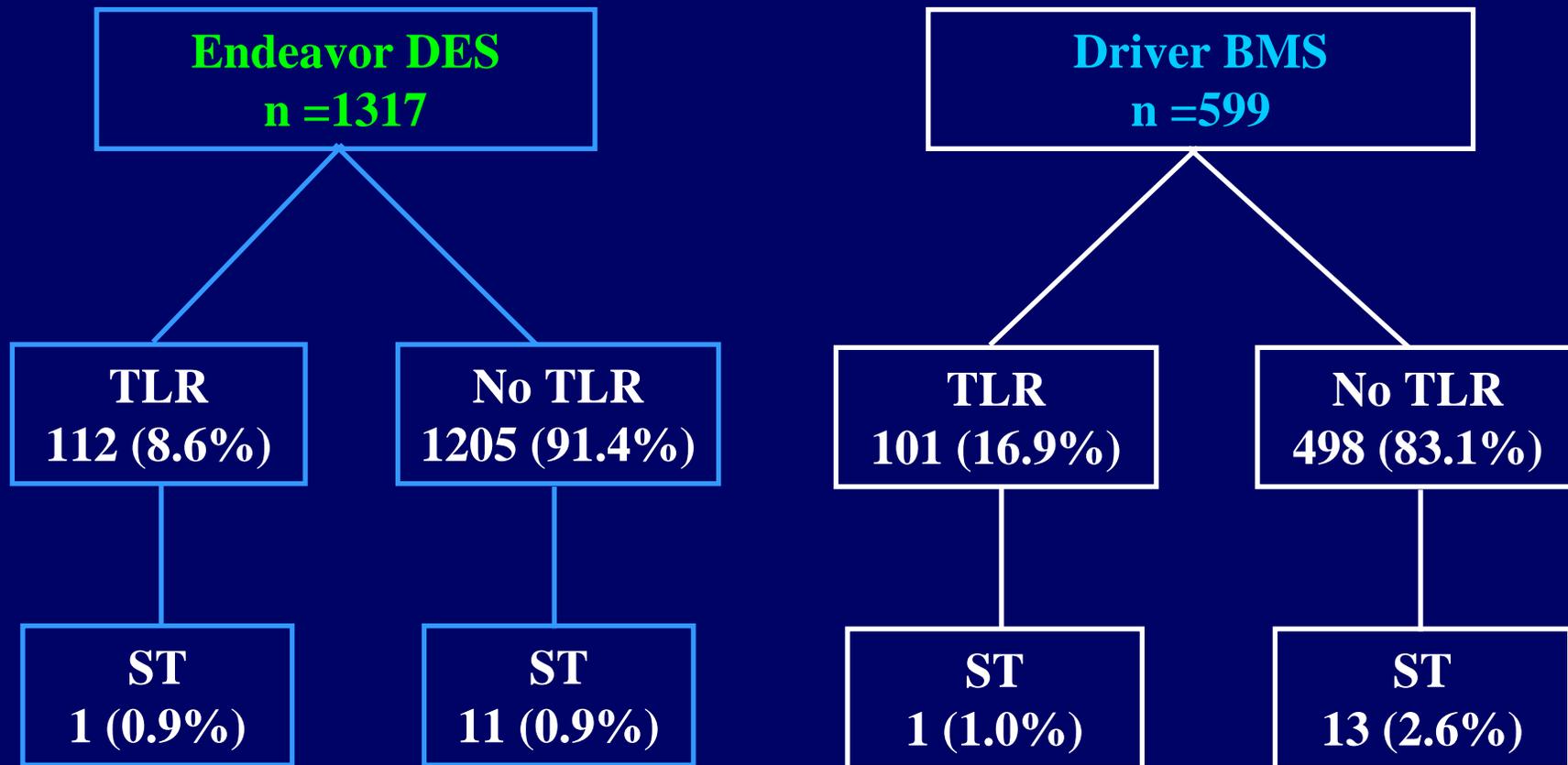
ENDEAVOR II

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.