SORT OUT III

Perspectives on 18-Month Results

SORT OUT III Perspectives

- **<u>Concerns with SORT OUT III Methodology</u>: The SORT OUT III study uses an unconventional methodology that raises questions regarding the reproducibility and viability of the results**

- **<u>Inconsistency of Data for Cypher DES</u>: SORT OUT III shows unexpectedly low rates and inconsistent data for Cypher compared with nearly every other trial utilizing the Cypher stent**

- **<u>SORT OUT III Results Are Short-Term Only</u>: The long-term deficiencies of Cypher demonstrated in multiple studies are not addressed by the short-term focus of SORT OUT III**

- **<u>Consistency of Data for Endeavor DES</u>: While the SORT OUT III data are inconsistent for Cypher, the Endeavor outcomes in SORT OUT III reinforce the low and durable event rates for the Endeavor stent**
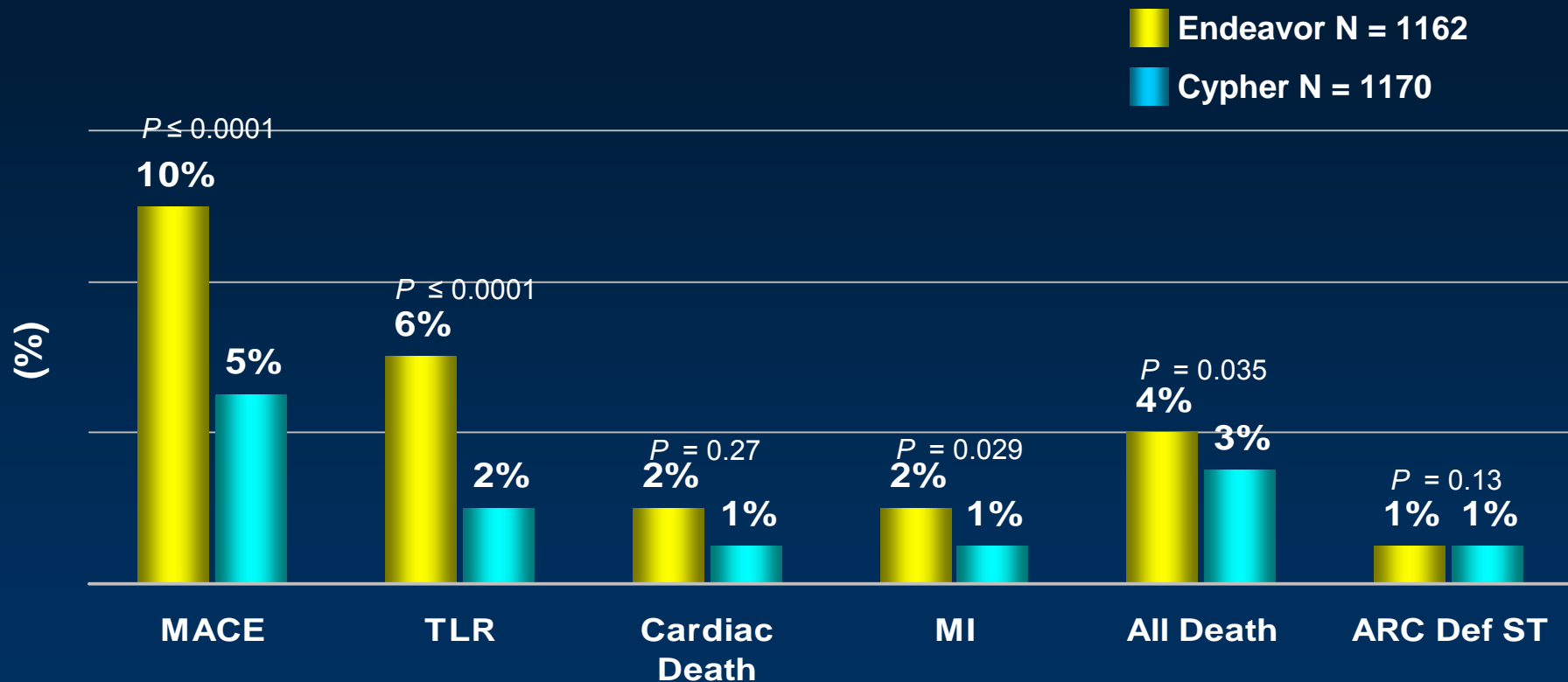
SORT OUT III
Questionable Trial Methodology

1. Positioned as a randomized "real-world" study yet nearly 60% (3344) of eligible patients were excluded in the analysis

2. Unlike controlled trials with rigorous patient follow-up, SORT OUT III is dependent on patient records from a national database

3. Investigators themselves—not an independent clinical events committee–-determined and verified stent thrombosis (ST), target lesion revascularization (TLR), myocardial infarction (MI) and restenosis

4. Procedure-related MIs were not captured, which may introduce bias because other studies utilizing these two stents have demonstrated a high rate of periprocedural MIs with Cypher and a low rate with Endeavor[1]

5. Differences in patient adherence to DAPT regimens were not reported despite the potential effect on safety outcomes

[1] In-Hospital MI rates: Cypher 2.3%, BMS 1.5% (SIRIUS Trial); Cypher 3.5%, Endeavor 0.6% (ENDEAVOR III Trial)

SORT OUT III
Event Rates at 18 Months

Legend:
- Endeavor N = 1162
- Cypher N = 1170

(%)

	MACE	TLR	Cardiac Death	MI	All Death	ARC Def ST
P-value	P ≤ 0.0001	P ≤ 0.0001	P = 0.27	P = 0.029	P = 0.035	P = 0.13
Endeavor	10%	6%	2%	2%	4%	1%
Cypher	5%	2%	1%	1%	3%	1%

- **The MACE and MI rates in SORT OUT III exclude periprocedural MI**
- **In ENDEAVOR III procedural MI = Cypher 3.5% *vs.* Endeavor 0.6% (p =0.042); therefore the impact on the MACE and MI rates in SORT OUT III is unknown**

Rasmussen K et al. Lancet, Published Online March 15, 2010

Cypher: SORT OUT III TLR
Inconsistent Clinical Evidence

18 Months

12 Months

7.3%

5.8%

4.9%

4.5%

4.3%

2.0%

(%)

SORT OUT III[1]
N = 1170

SORT OUT II[2]
N = 1065

LEADERS[3]
N = 850

SIRTAX[4]
N = 500

SIRIUS[5]
N = 533

Cypher Pooled[6]
N = 878

[1] Rasmussen K et al. Lancet, Published Online March 15, 2010
[2] Galloe AM et al., JAMA, 299:4 pp. 409-416, 2008.
[3] Klaus V et al., TCT 2009
[4] Räber L et al., TCT2009
[5] Weisz G et al., JACC, 53 pp. 1488-1497, 2009.
[6] Caixeta A et al., JACC, 54 pp. 894-902, 2009.

Cypher: SORT OUT III MACE
Inconsistent Clinical Evidence

18 Months

12 Months

12.1%

10.0%

8.4% 8.3%

7.1%

5.0%

(%)

| SORT OUT III[1] | SORT OUT II[2] | LEADERS[3] | SIRTAX[4] | SIRIUS[5] | Cypher Pooled[6] |
| N = 1170 | N = 1065 | N = 850 | N = 500 | N = 533 | N = 878 |

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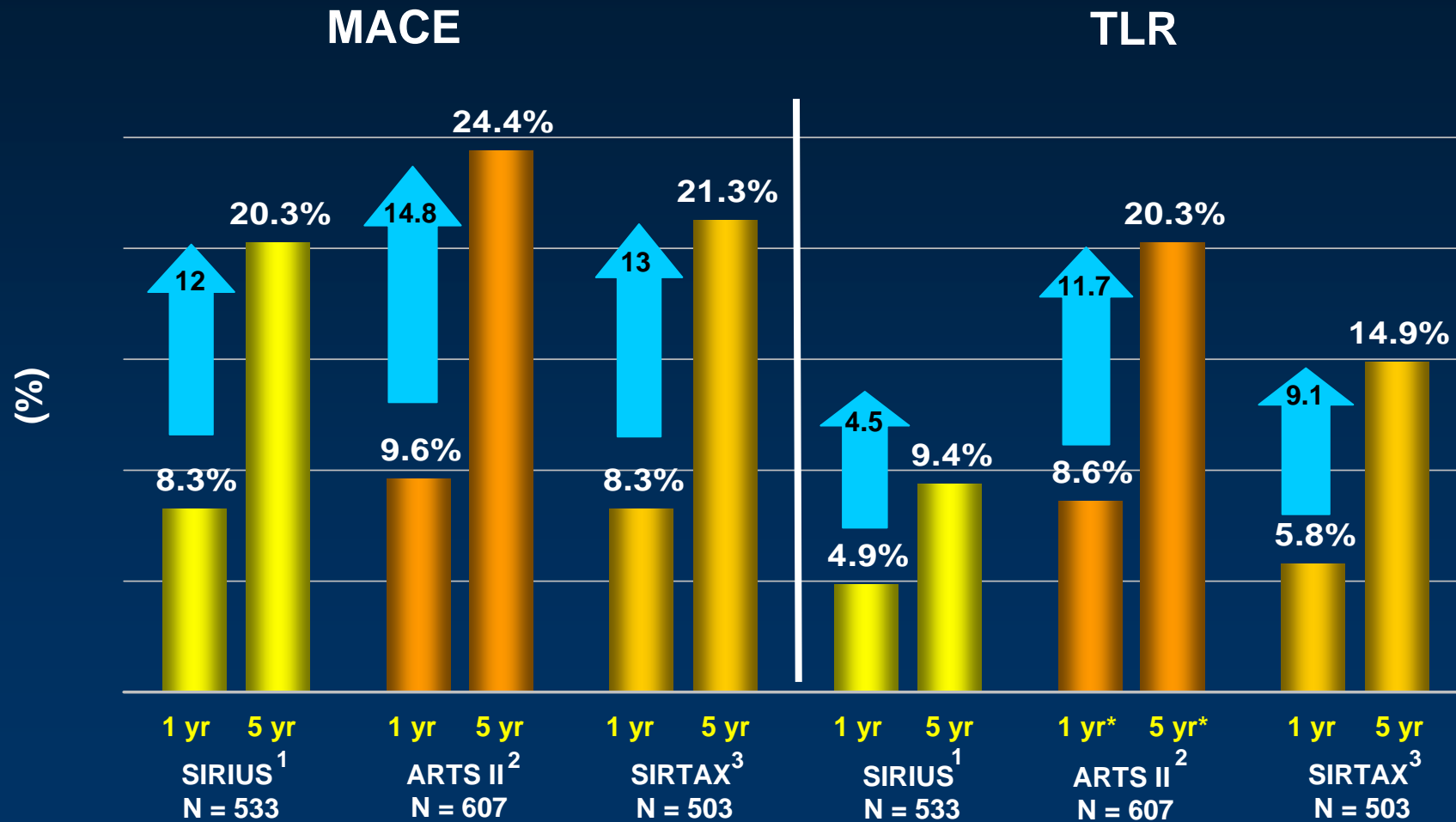[3] Klaus V et al., TCT 2009
[4] Räber L et al., TCT2009
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Cypher: Long-Term Endpoint Increases
MACE and TLR Increase from 1 – 5 Yr

MACE

TLR

(%)

MACE:
- SIRIUS[1] N = 533: 1 yr 8.3%, 5 yr 20.3%, increase 12
- ARTS II[2] N = 607: 1 yr 9.6%, 5 yr 24.4%, increase 14.8
- SIRTAX[3] N = 503: 1 yr 8.3%, 5 yr 21.3%, increase 13

TLR:
- SIRIUS[1] N = 533: 1 yr 4.9%, 5 yr 9.4%, increase 4.5
- ARTS II[2] N = 607: 1 yr* 8.6%, 5 yr* 20.3%, increase 11.7
- SIRTAX[3] N = 503: 1 yr 5.8%, 5 yr 14.9%, increase 9.1

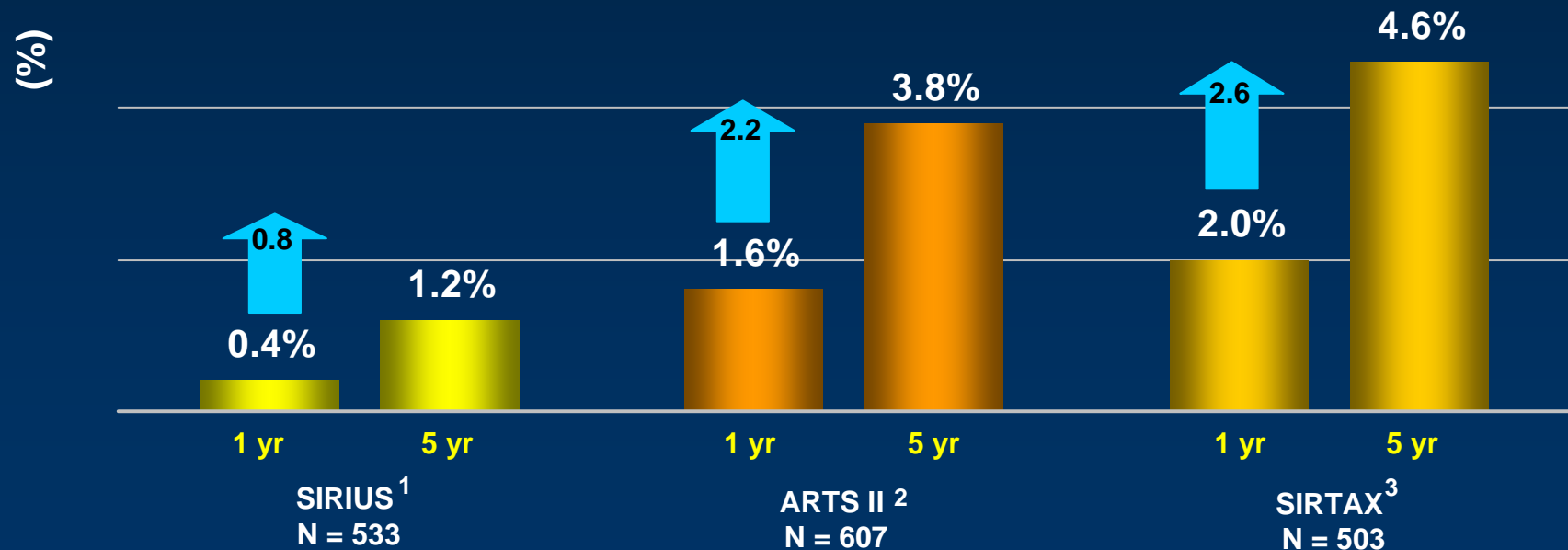[1] Weisz G et al., JACC, 53 pp. 1488-1497, 2009.
[2] Serruys P et al., EuroInterv, 1 pp. 147-156, 2005. Serruys P et al., JACC, 55 pp. 1093-1101, 2010.
[3] Räber L et al., TCT2009

* Total revascularization

Cypher: Long-Term Endpoint Increases
ARC Definite ST Increases from 1 – 5 Yr

(%)

SIRIUS: 1 yr 0.4%, 5 yr 1.2% (+0.8)
ARTS II: 1 yr 1.6%, 5 yr 3.8% (+2.2)
SIRTAX: 1 yr 2.0%, 5 yr 4.6% (+2.6)

SIRIUS [1]
N = 533

ARTS II [2]
N = 607
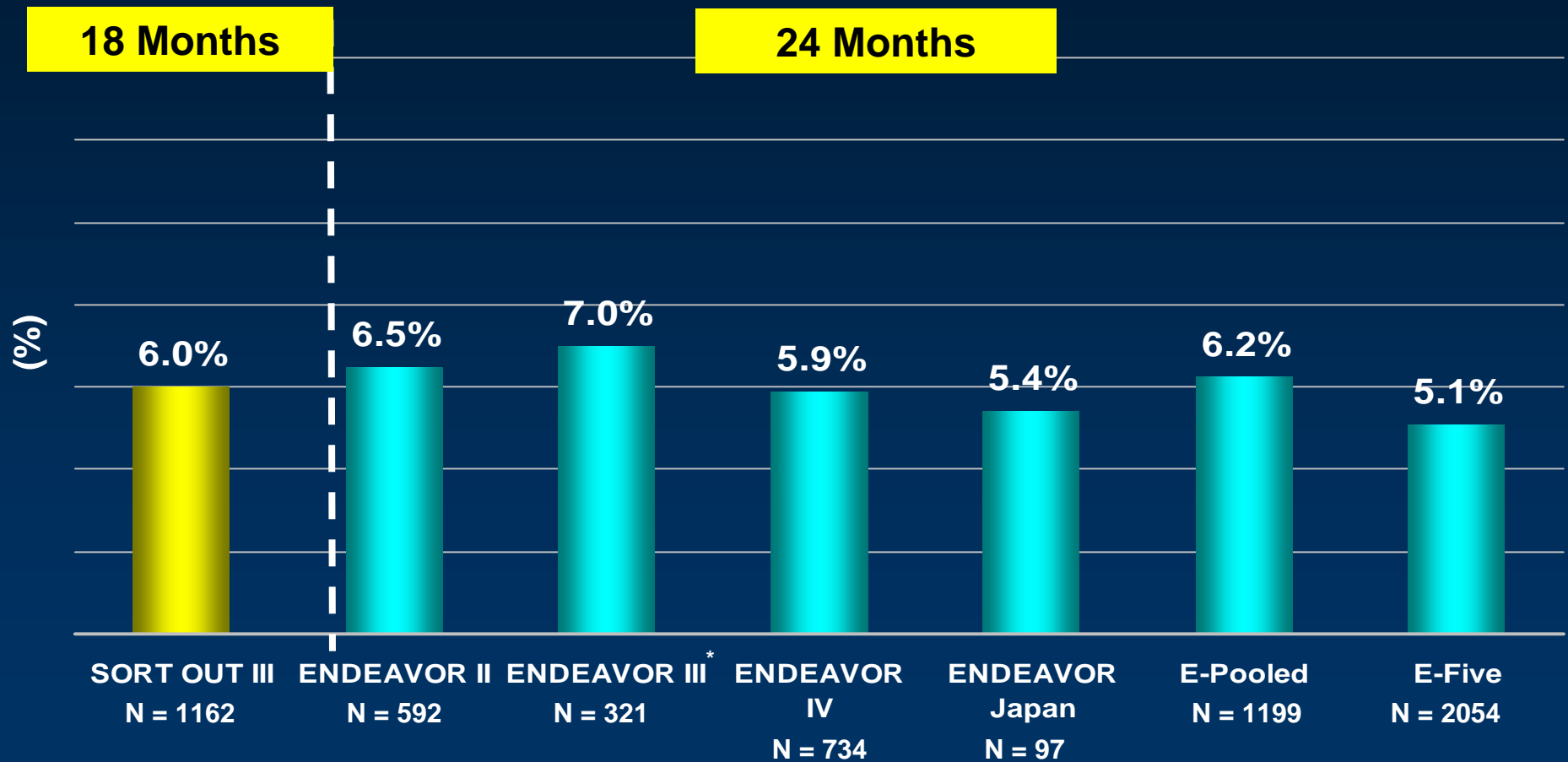
SIRTAX [3]
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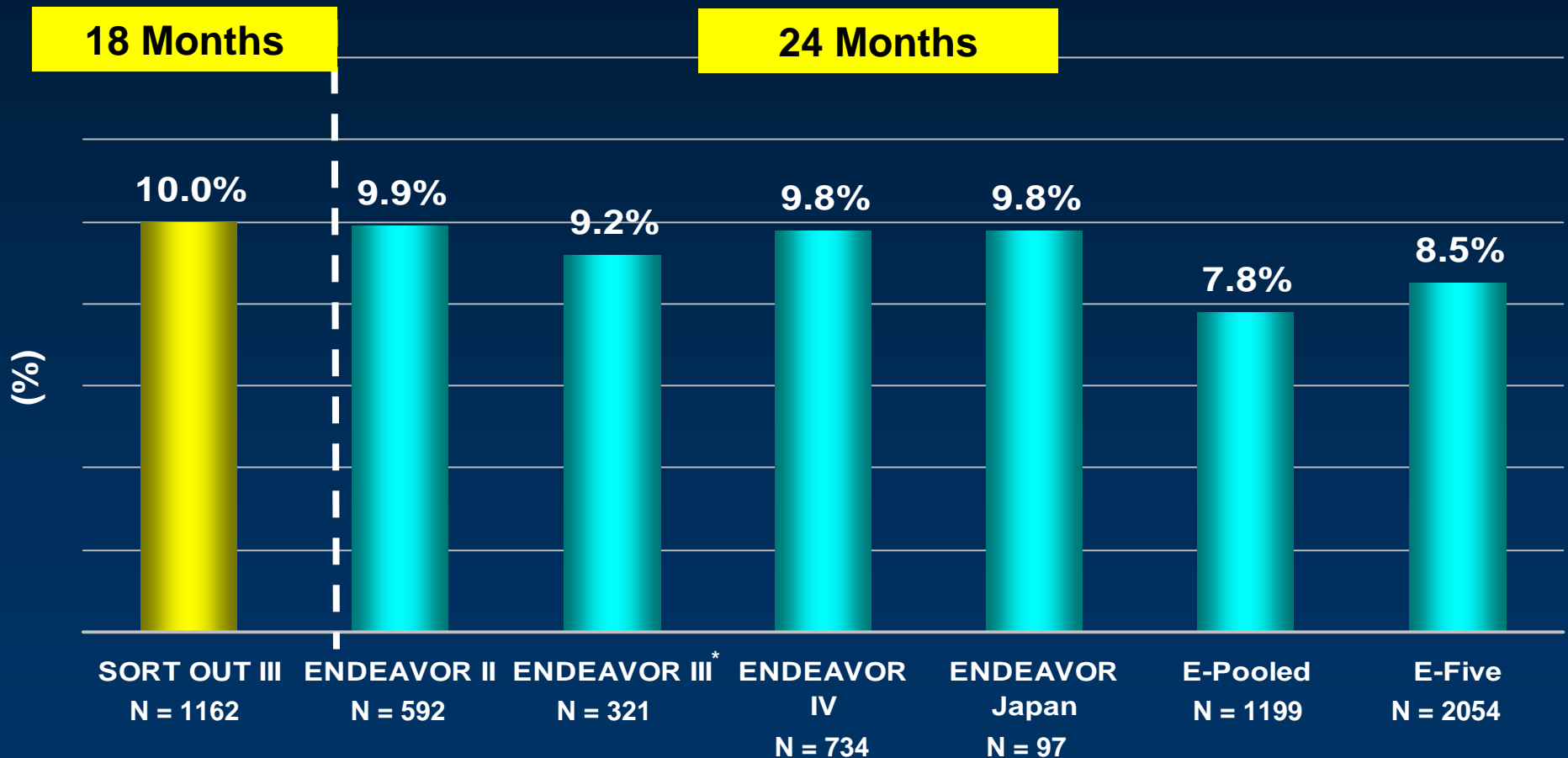
Endeavor: SORT OUT III TLR
Consistent Clinical Evidence

18 Months | 24 Months

(%)

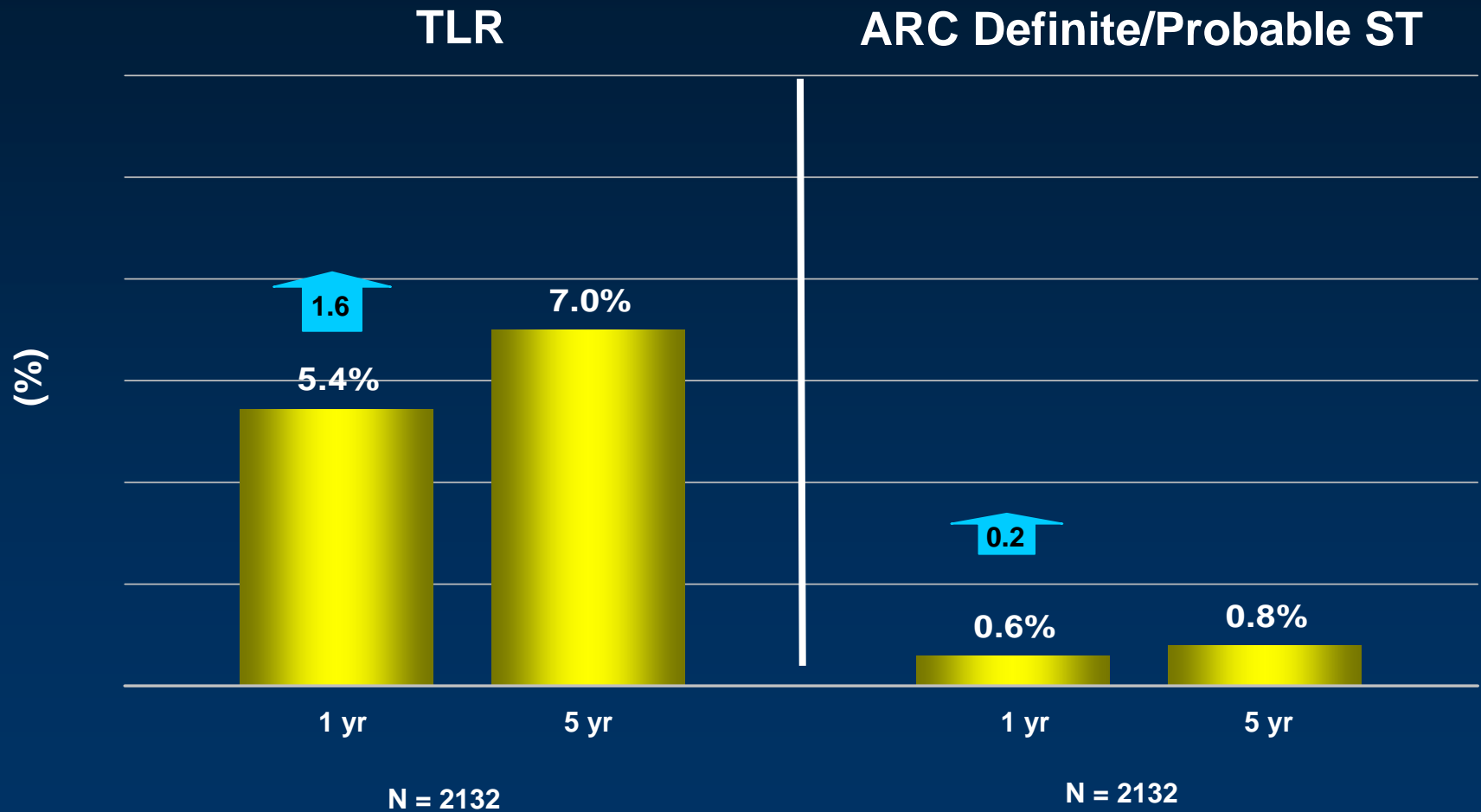| Study	Value
SORT OUT III (N = 1162)	6.0%
ENDEAVOR II (N = 592)	6.5%
ENDEAVOR III* (N = 321)	7.0%
ENDEAVOR IV (N = 734)	5.9%
ENDEAVOR Japan (N = 97)	5.4%
E-Pooled (N = 1199)	6.2%
E-Five (N = 2054)	5.1%

* ENDEAVOR III included angiographic follow-up in all patients.
ENDEAVOR Pooled Analysis: E I (5 yr), E II (5 yr), E II CA (5 yr), E III (5 yr), E IV (3 yr) and E pK (3 yr).

Endeavor: SORT OUT III MACE
Consistent Clinical Evidence

18 Months

24 Months

(%)

10.0%	9.9%	9.2%	9.8%	9.8%	7.8%	8.5%
SORT OUT III	ENDEAVOR II	ENDEAVOR III*	ENDEAVOR IV	ENDEAVOR Japan	E-Pooled	E-Five
N = 1162	N = 592	N = 321	N = 734	N = 97	N = 1199	N = 2054

* ENDEAVOR III included angiographic follow-up in all patients.
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ENDEAVOR Pooled Analysis
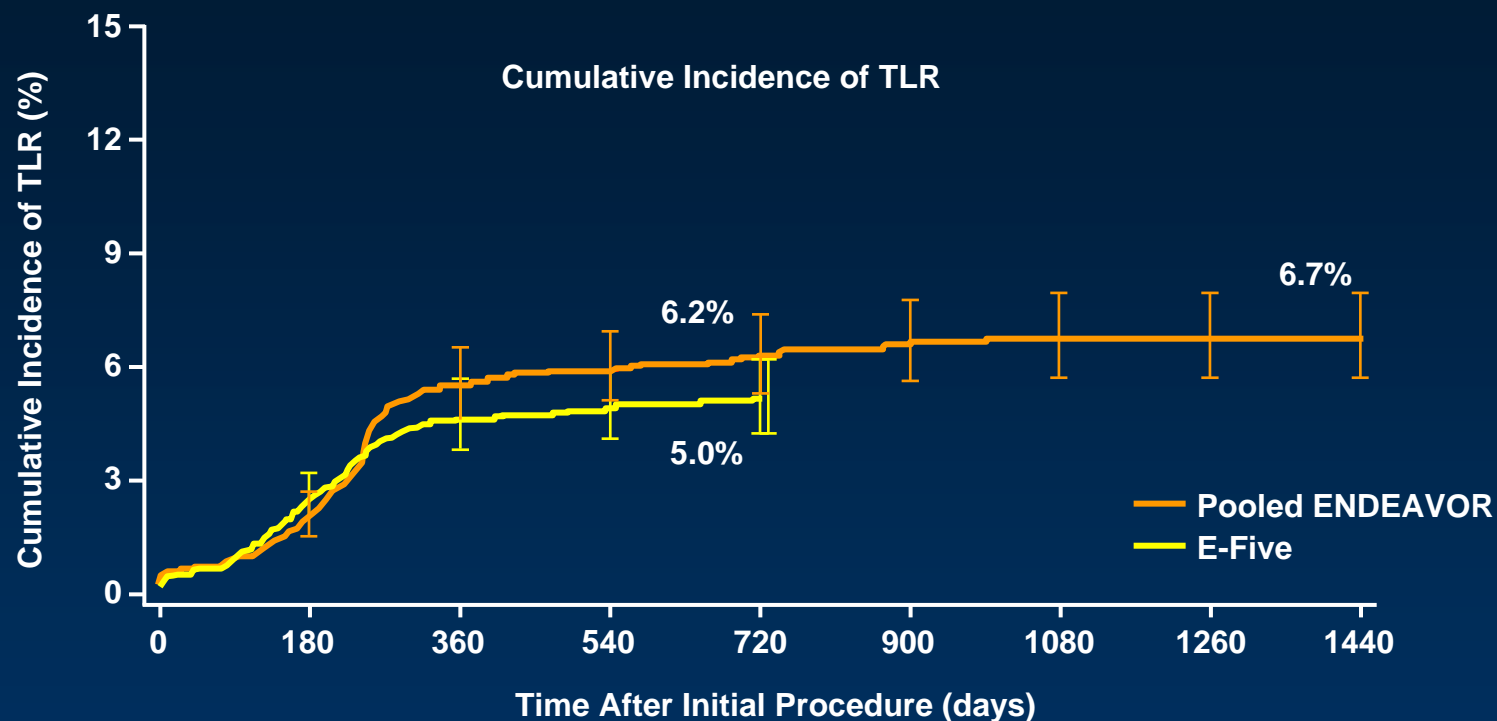## *TLR and ARC Def/Prob ST From 1 – 5 Yr*

SORT OUT III Perspectives

- **Concerns with SORT OUT III Methodology:** The SORT OUT III study uses an unconventional methodology that raises questions regarding the reproducibility and viability of the results

- **Inconsistency of Data for Cypher:** SORT OUT III shows unexpectedly low rates and inconsistent data for Cypher compared with nearly every other trial utilizing the Cypher stent

- **SORT OUT III Results Are Short-Term Only:** The long-term deficiencies of Cypher demonstrated in multiple studies are not addressed by the short-term focus of SORT OUT III

- **Consistency of Data for Endeavor:** While the SORT OUT III data are inconsistent for Cypher, the Endeavor outcomes in SORT OUT III reinforce the low and durable event rates for the Endeavor stent

Endeavor: Durable TLR Rates
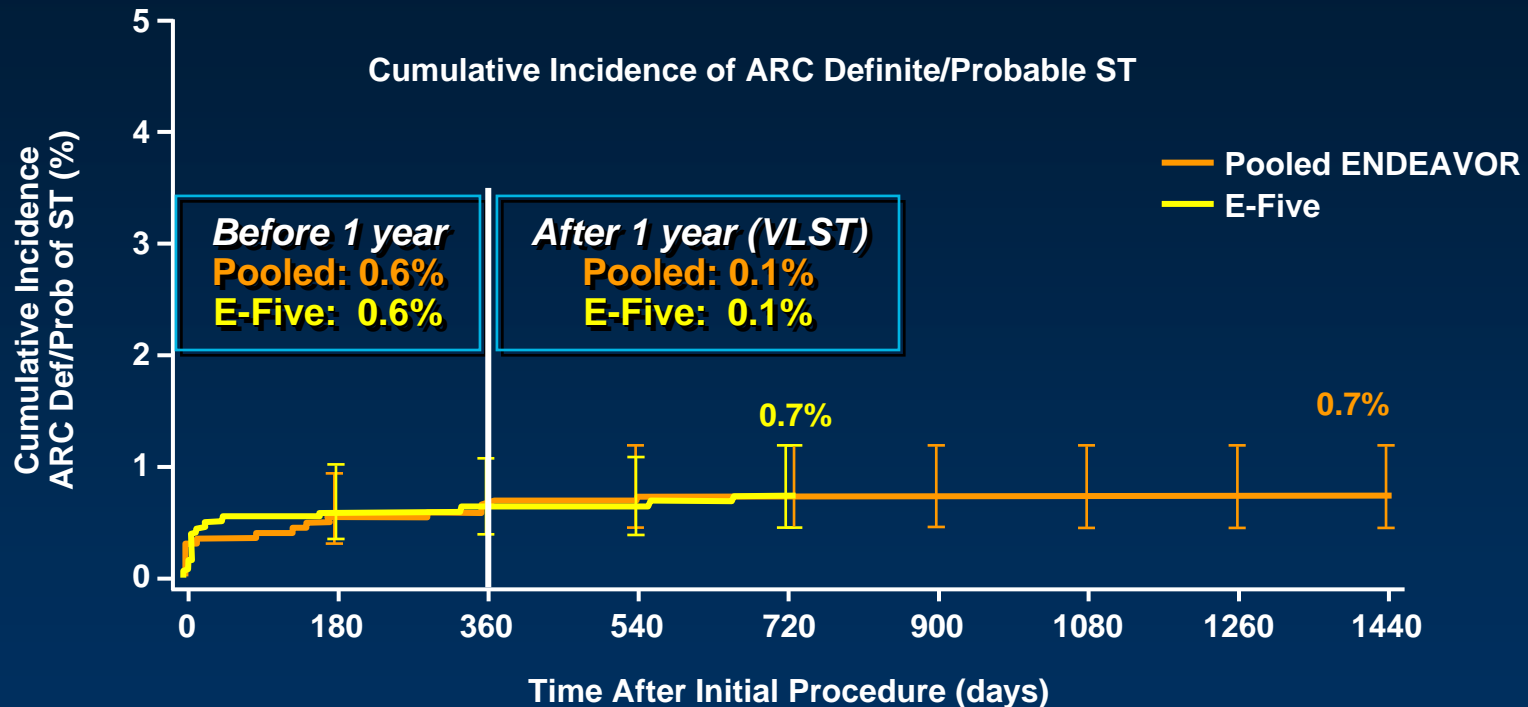## Real-World Experience Consistent with Pooled Analysis

Cumulative Incidence of TLR

Cumulative Incidence of TLR (%)

6.7%

6.2%

5.0%

— Pooled ENDEAVOR
— E-Five

Time After Initial Procedure (days)

Days	0	180	360	540	720	730	900	1080	1260	1440
No. at Risk	2133	2130	2061	1939	1895	1557	1169	1150	1015	858
% CI	0.1	1.8	5.4	5.8	6.2	6.2	6.5	6.7	6.7	6.7
No. at Risk	2116	2113	2046	1974	1924	1816				
% CI	0.0	2.3	4.5	4.8	5.0	5.0				

ENDEAVOR Pooled Analysis: E I (5 yr), E II (4 yr), E II CA (4 yr), E III (3 yr), E IV (2 yr) and E pK (2 yr).
The 2-year follow-up rate for Pooled Analysis was measured at 720 days and for E-Five at 730 days.

Endeavor: Low Rates of ARC Def/Prob ST
Real-World Experience Consistent with Pooled Analysis

Cumulative Incidence of ARC Definite/Probable ST

Cumulative Incidence ARC Def/Prob of ST (%)

Before 1 year
Pooled: 0.6%
E-Five: 0.6%

After 1 year (VLST)
Pooled: 0.1%
E-Five: 0.1%

0.7%

0.7%

— Pooled ENDEAVOR
— E-Five

Time After Initial Procedure (days)

Days	0	180	360	540	720	730	900	1080	1260	1440
No. at Risk	2133	2131	2089	2036	1995	1650	1241	1225	1087	909
% CI	0.0	0.5	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.7
No. at Risk	2116	2113	2086	2060	2014	1906				
% CI	0.0	0.6	0.6	0.6	0.7	0.7				

ENDEAVOR Pooled Analysis: E I (5 yr), E II (4 yr), E II CA (4 yr), E III (3 yr), E IV (2 yr) and E pK (2 yr).
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