

Duration of DAPT after (new) DES

Is 3 months enough?

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Disclosure Statement of Financial Interest

I, **SORIN BRENER MD**, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Stent Thrombosis

- The most feared complication of PCI with stenting is ST
- ST results in ACS in majority of patients, although slowly progressive restenosis with eventual thrombosis and without ACS may also occur.
- Early ST results in higher mortality than late and very late ST – for unknown reasons

Kimura T et al. Circulation 2010;122:52-61

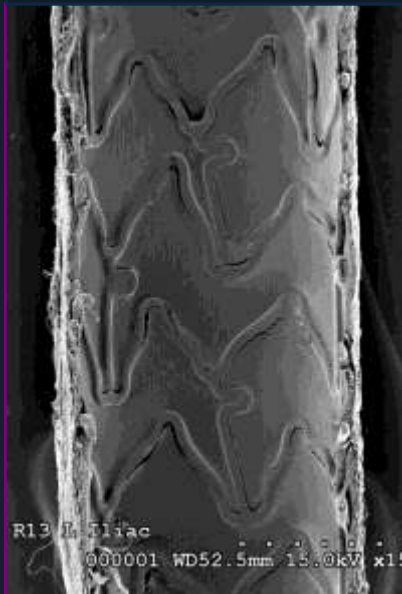
Armstrong EJ et al. JACC Cardiovasc Interv 2012;5:131-40

Not all DES are created equal...

- **The potential for ST depends on:**
 - **Strut material**
 - **PCI milieu (ACS)**
 - **Composition and persistence of polymer**
 - **Recovery of endothelial function**
 - **Duration of DAPT**
 - **Comorbidities**
 - **Diabetes**
 - **CKD**

14 Day Endothelialization: Rabbit Iliac Model

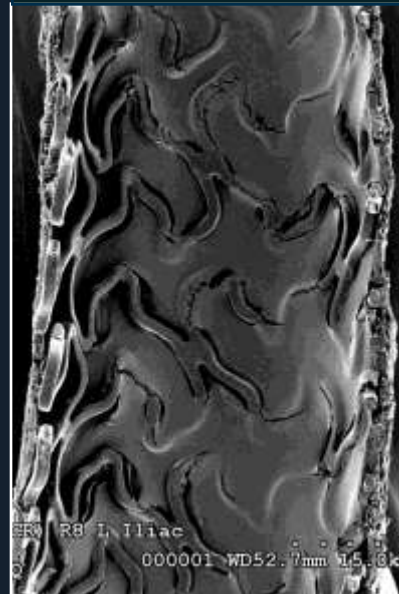
XIENCE V



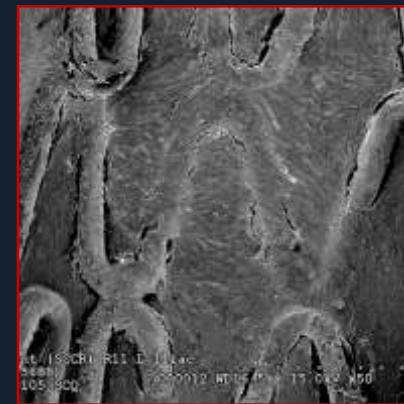
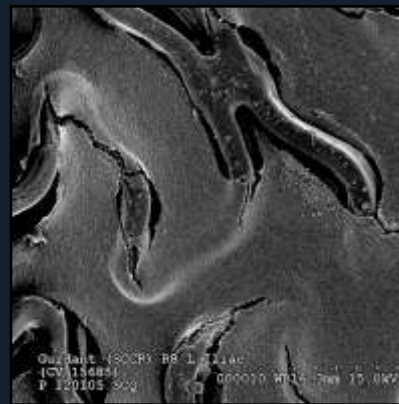
CYPHER



TAXUS



ENDEAVOR

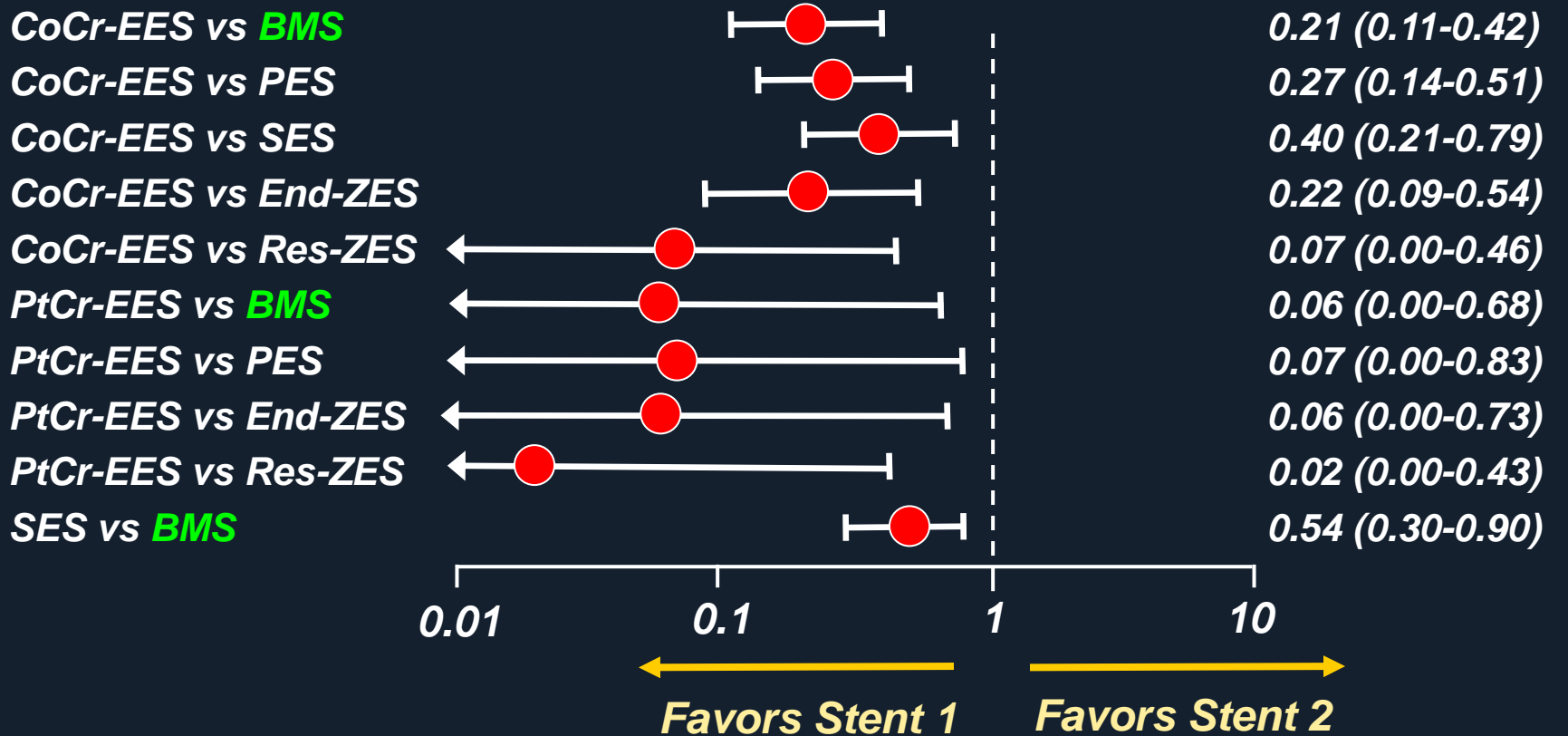


Stent Thrombosis Network Meta-analysis

ARC Definite ST

49 RCTs, 50,844 pts

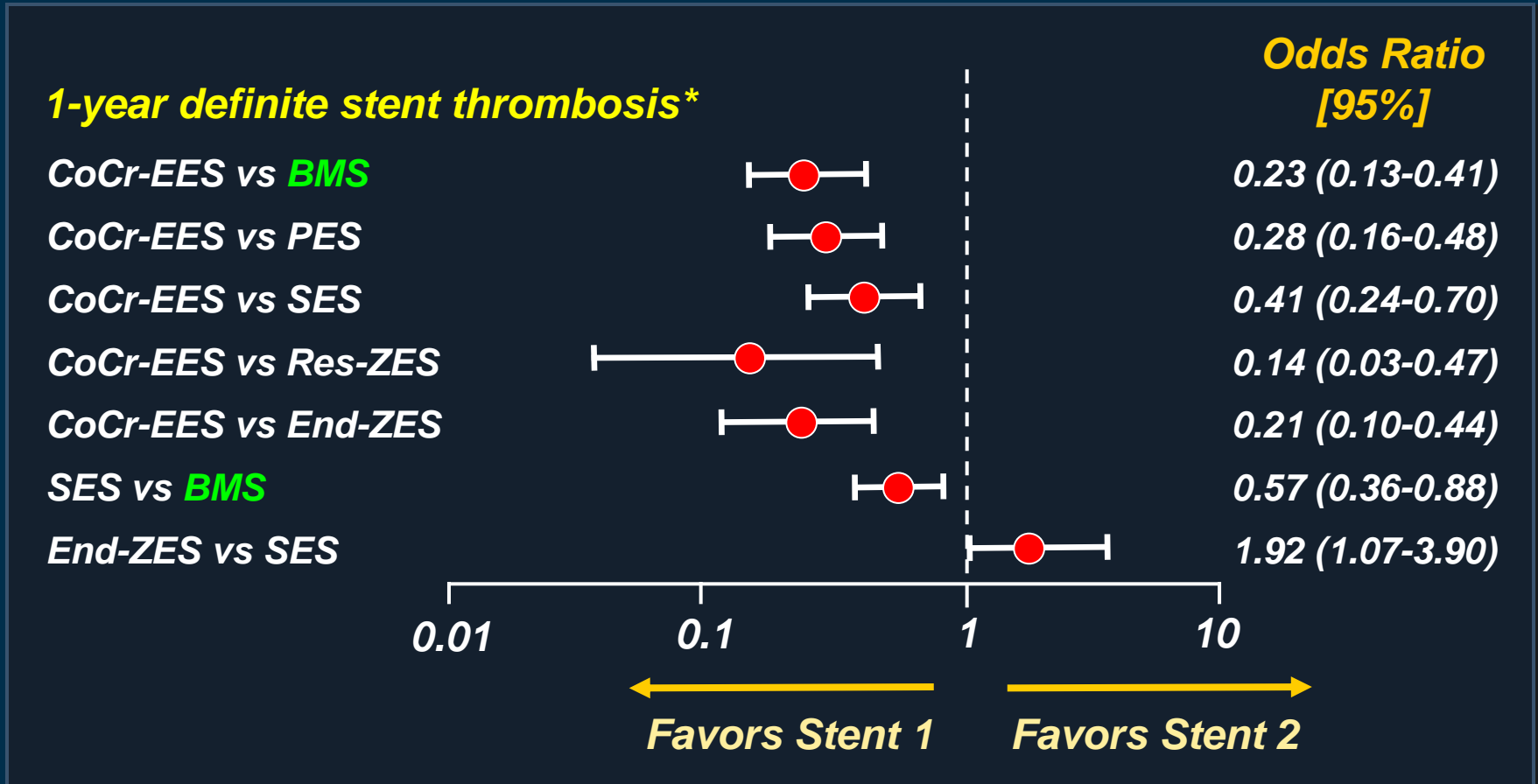
30-day definite stent thrombosis*



Stent Thrombosis Network Meta-analysis

ARC Definite ST

49 RCTs, 50,844 pts



Why consider shorter DAPT duration after DES?

- The current recommendations are based on arbitrary duration of therapy from G1-DES trials
- Risk of bleeding increase with DAPT duration
- Unanticipated need for DAPT interruption is frequent
- Prolonged DAPT (>1 year) is not beneficial

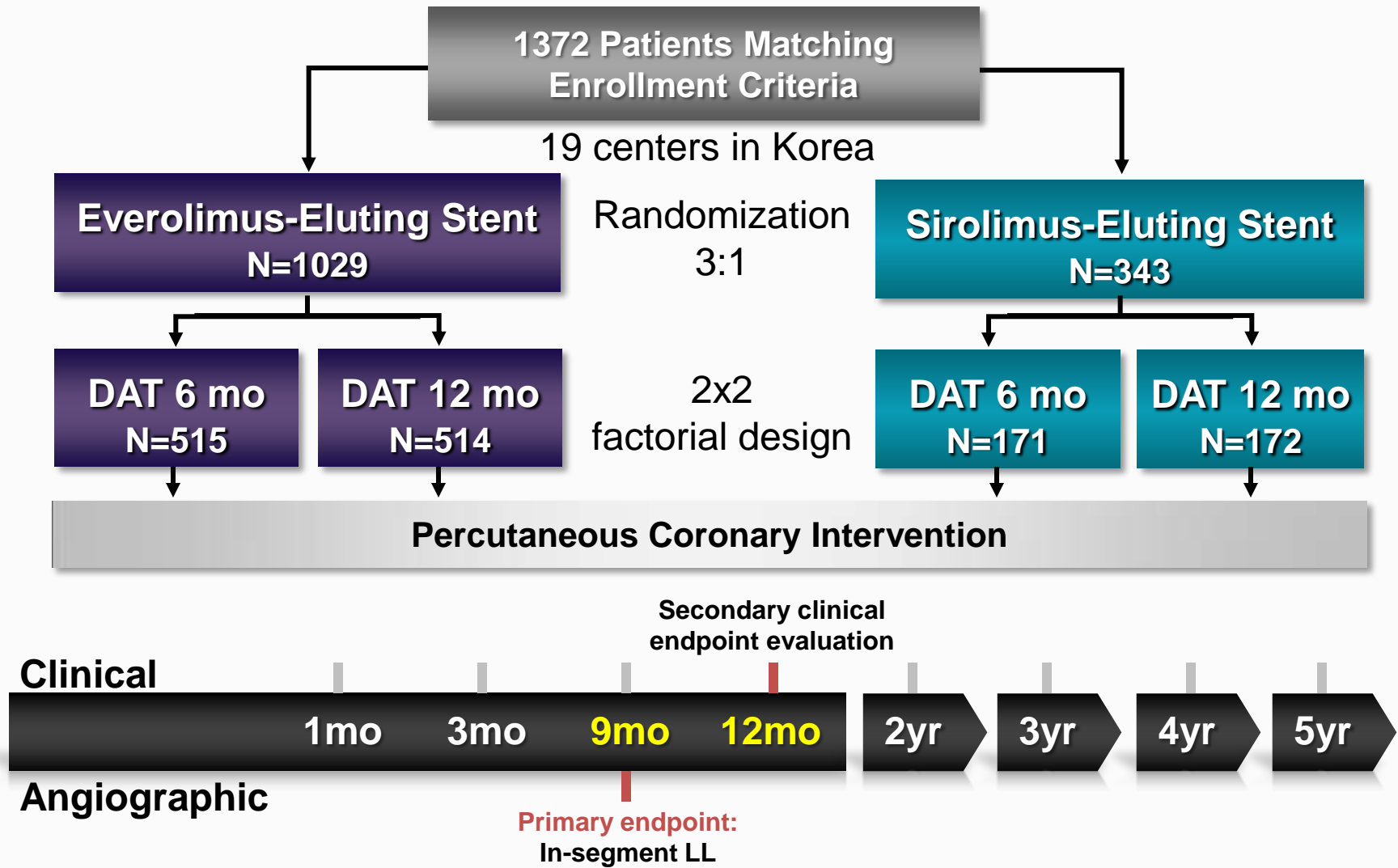
Park SJ et al. N Engl J Med 2010;362:1374-82.

Cassese S et al. European Heart Journal 2012;33:3078-3087.

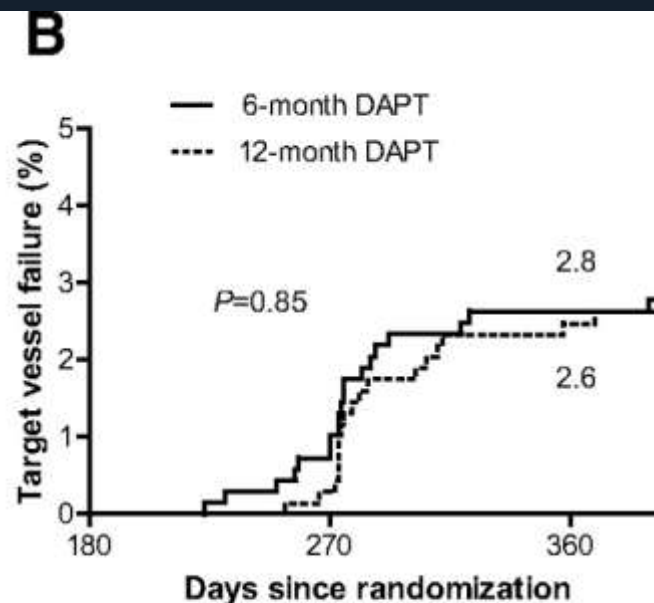
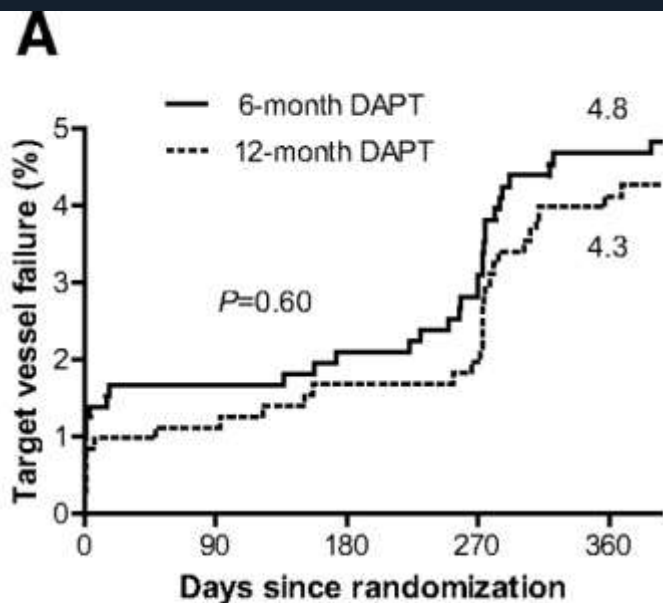
Mehran R et al. The Lancet 2013;382:1714-1722.

Trial Design

Prospective, open label, two-arm, randomized multi-center trial

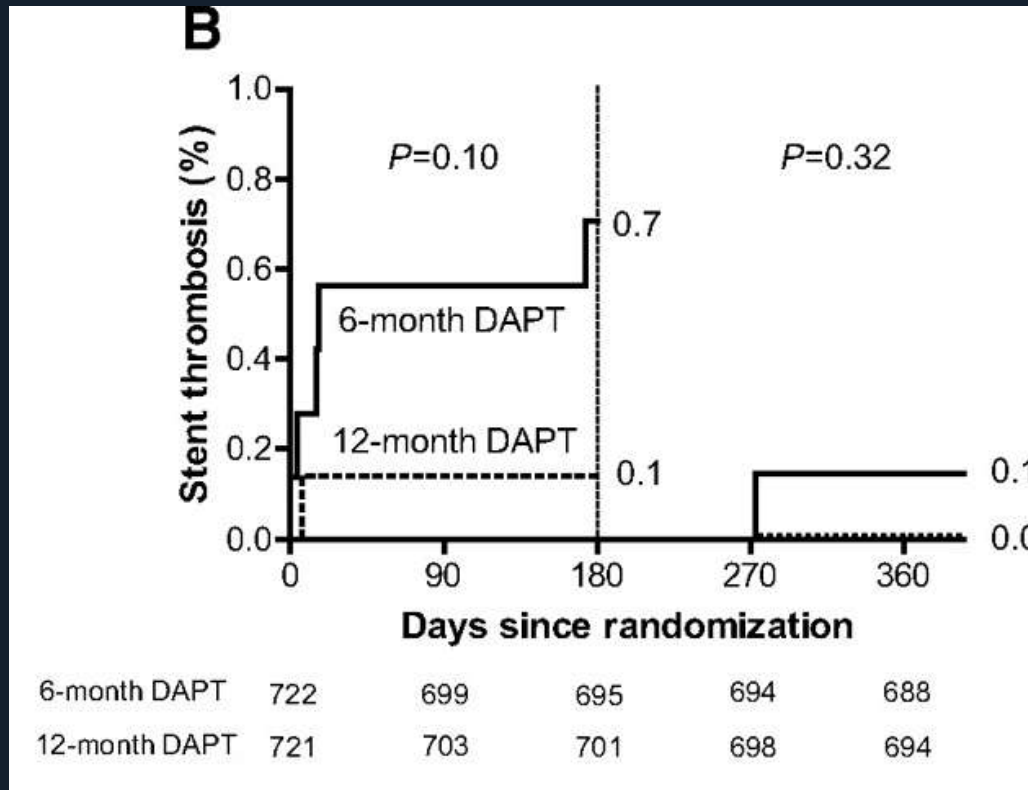


Target Vessel Failure



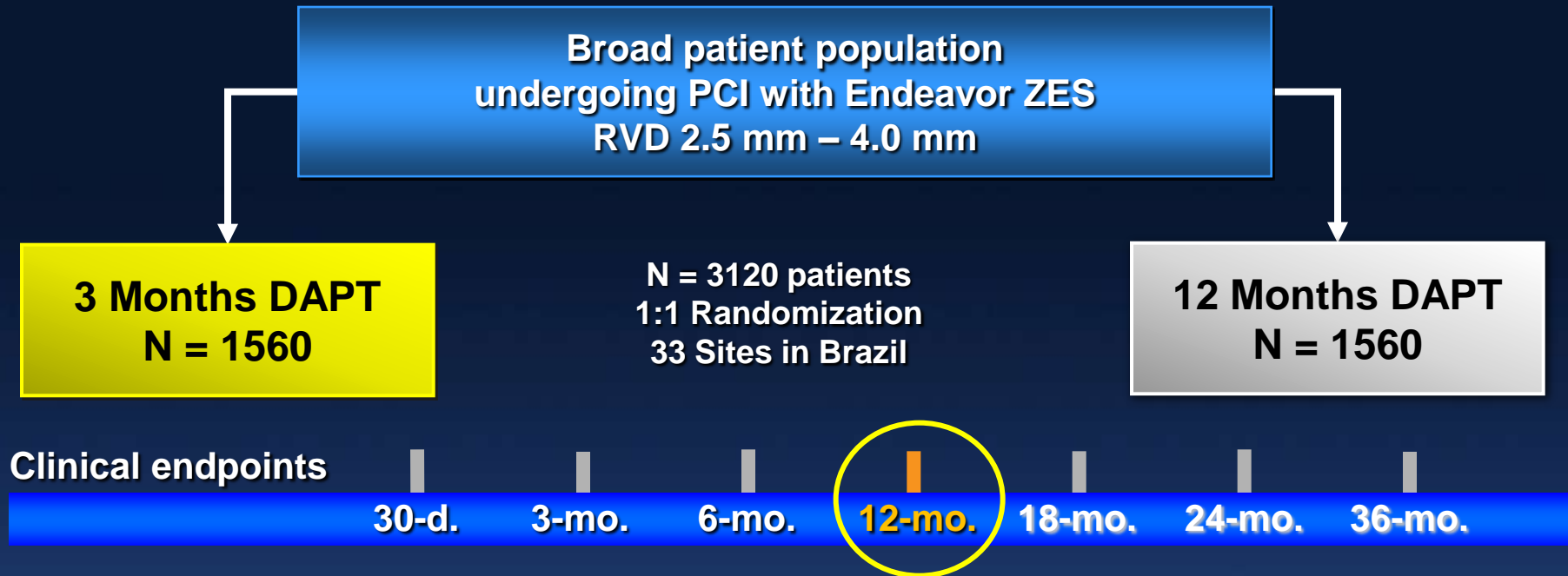
6-month DAPT	722	692	686	680	663	6-month DAPT	686	680	663
12-month DAPT	721	697	692	687	668	12-month DAPT	692	687	668

Stent Thrombosis



Gwon HC et al. *Circulation* 2012;125:505-13.

Study Design



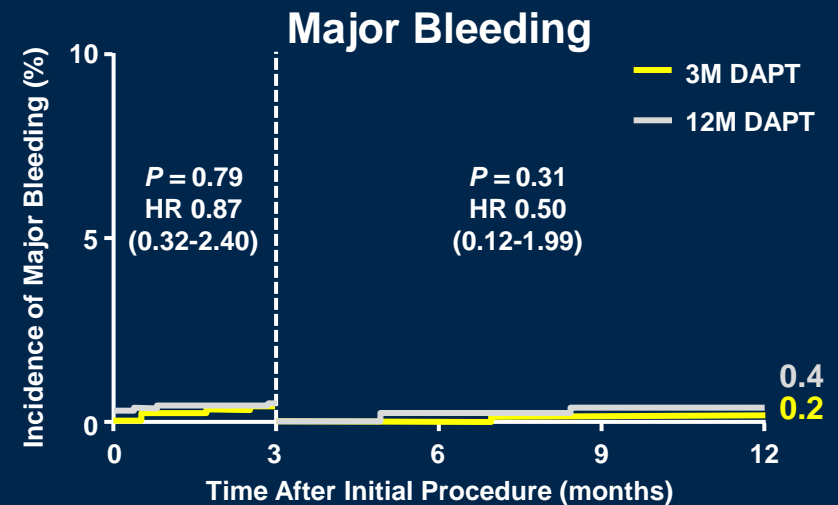
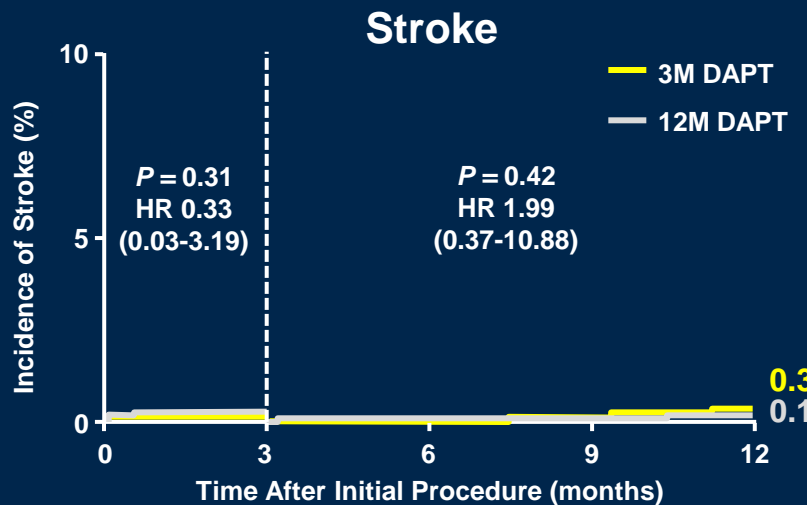
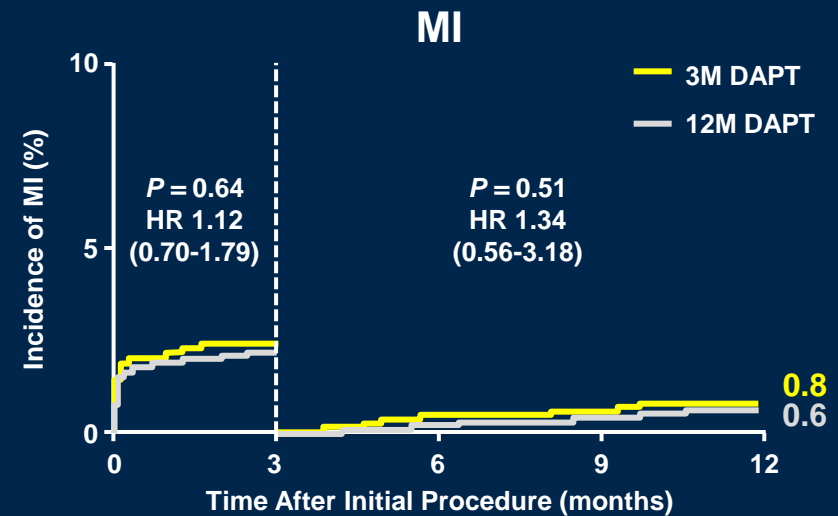
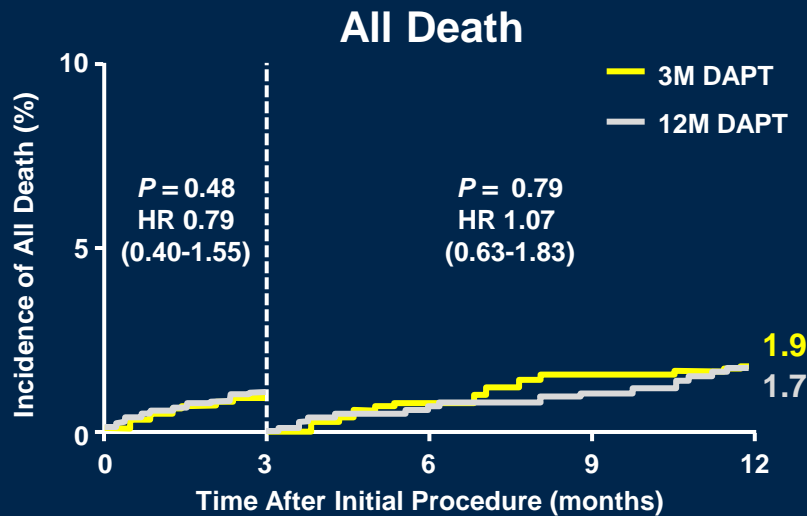
Primary Endpoint: NACCE (Death / MI / Stroke / Major Bleeding) at 12 months

Secondary Endpoints: ARC defined ST, TVR, TLR, MACE, DAPT compliance, and major bleeding (REPLACE-2 & GUSTO definitions)

NACCE = Net Adverse Clinical and Cerebral Events

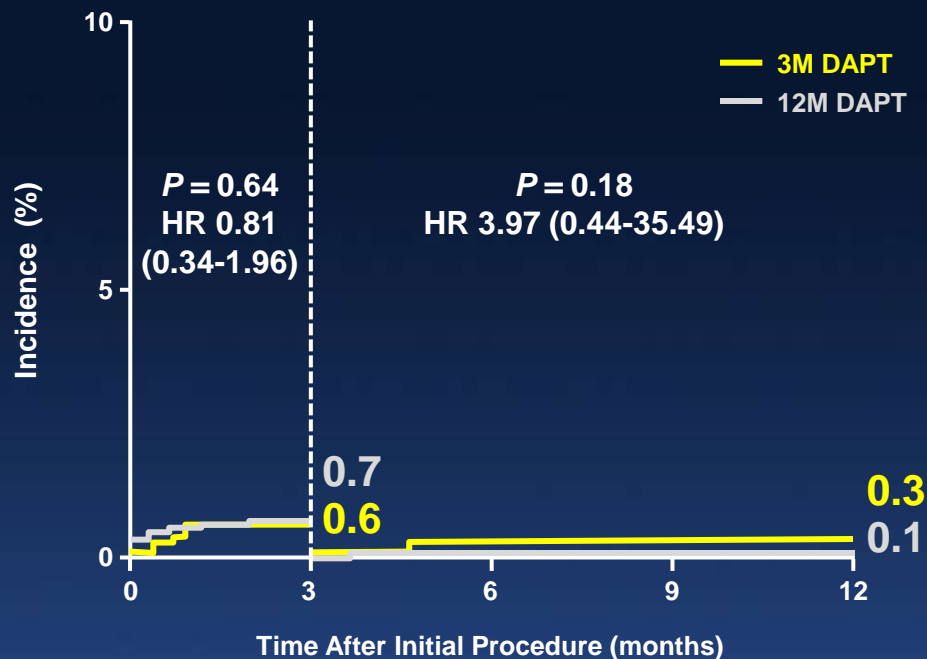
MACE is composed of Death, MI, Emergent CABG, TLR

NACCE Components – Landmark

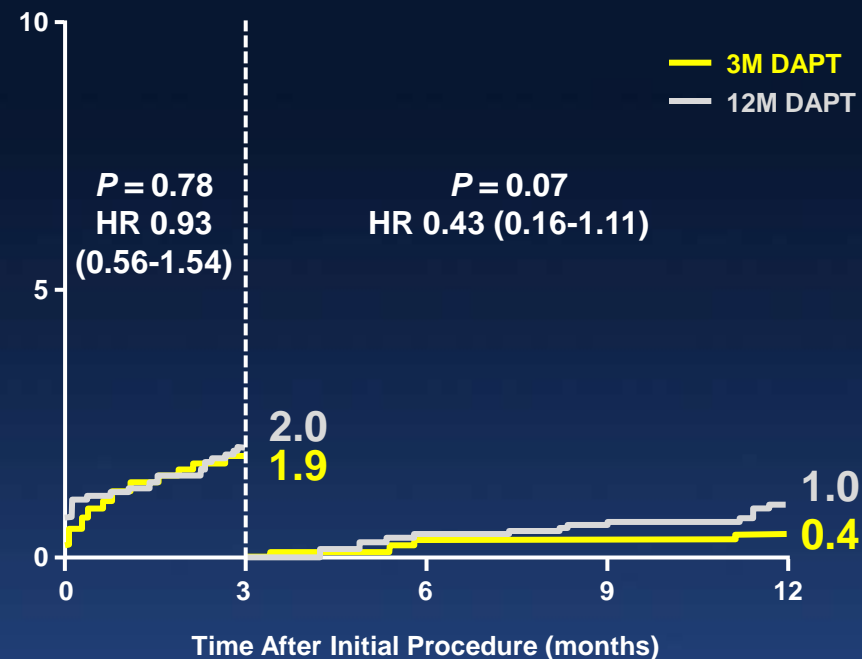


Stent Thrombosis vs. Bleeding

ARC Def./Prob. Stent Thrombosis



Any Bleeding*



Month	0	1	3	6	12
No at risk	1563	1555	1540	1506	1505
No events	0	6	3	4	0
No at risk	1556	1541	1525	1501	1500
No events	5	3	3	1	0

Month	0	1	3	6	12
No at risk	1563	1538	1516	1482	1439
No events	4	15	10	4	2
No at risk	1556	1528	1501	1472	1387
No events	11	8	12	6	8

RESET

2,148 patients enrolled and randomized

- E-ZES + 3-month DAPT
- Standard Therapy:
Other DES with 12-month DAPT

Divided into 4 subsets and 1:1 randomization was performed.

31 patients excluded
- 16 Withdrawal of consent
- 15 Met exclusion criteria

E-ZES + 3-month DAPT (n=1059)

Standard therapy (n=1058)

Diabetes mellitus subset (N=292)

Acute coronary syndrome subset (N=601)

Short-length DES Subset (N=681)

Long-length DES Subset (N=543)

E-ZES (n=146)

R-ZES (n=146)

E-ZES (n=301)

R-ZES (n=300)

E-ZES (n=341)

SES (n=340)

E-ZES (n=271)

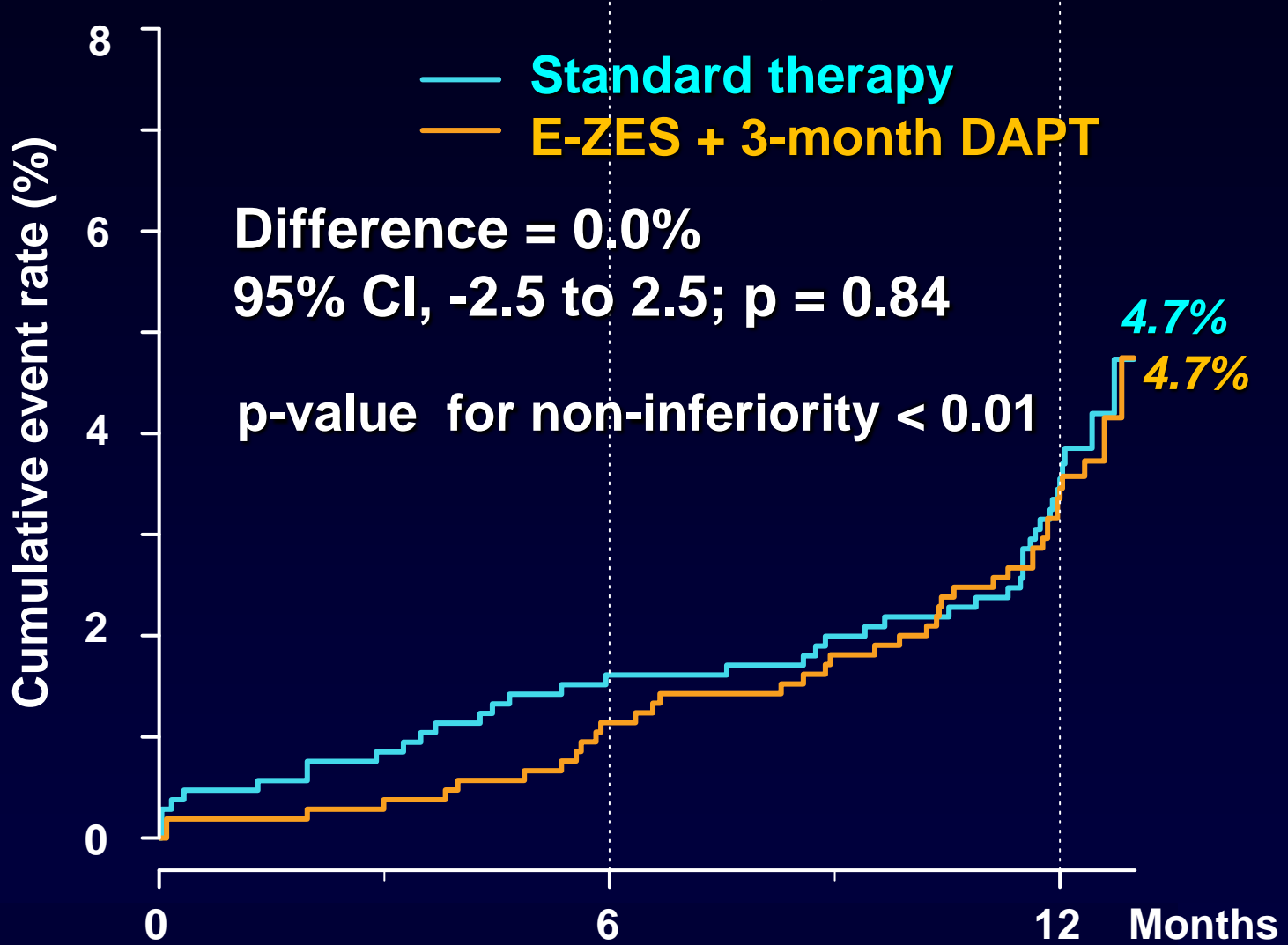
EES (n=272)

R-ZES = Resolute zotarolimus-eluting stent ; SES = sirolimus-eluting stent; EES = everolimus-eluting stents



CV death, MI, stent thrombosis, TVR or bleeding at 1 year

Kim BK et al. J Am Coll Cardiol 2012;60:1340-8.



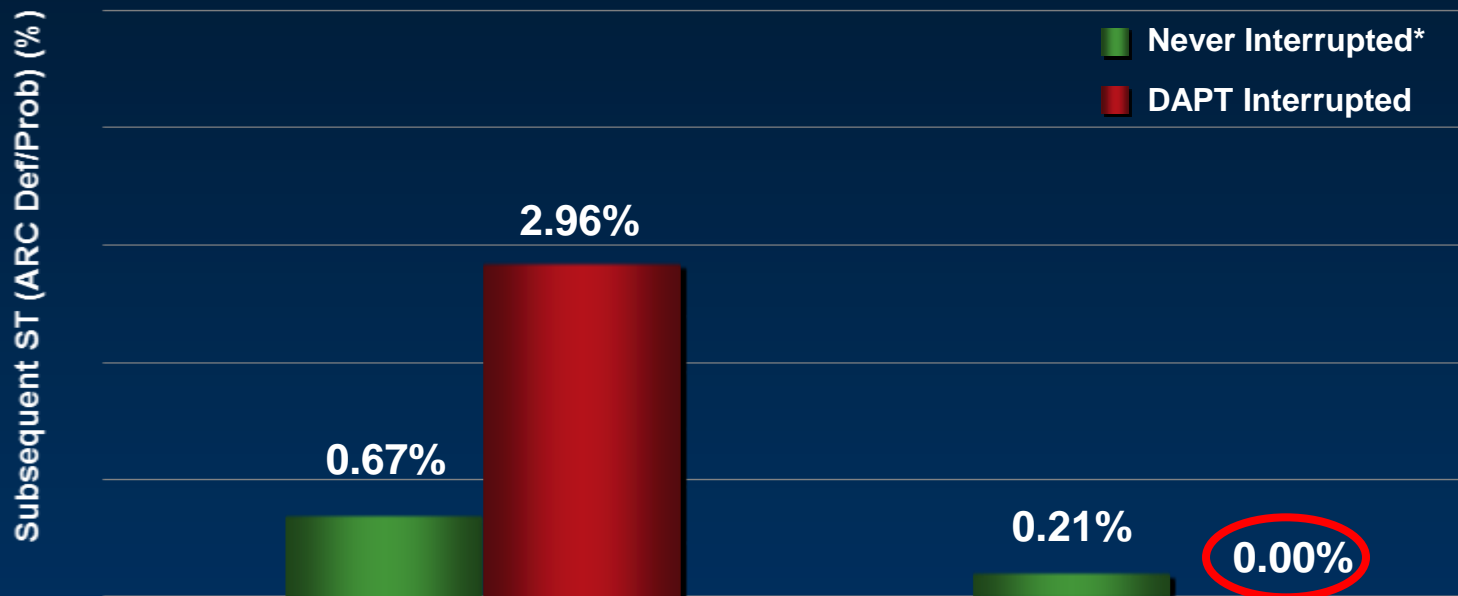
No. at Risk
E-ZES +3-month
DAPT
Standard therapy

0	6	12	Months
1059	1049	1037	1027
1058	1046	1032	1024
		945	920

RESOLUTE Pooled DAPT Interruption Analysis

Timing of First DAPT Interruption and ST Through 1 Year

1 Month



# of pts at risk at baseline	3,858	169	3,858	907 [‡]
# of events	26	5 [†]	8	0
# of days to interruption (median)	NA	3	NA	250
95% CI	[0.44%, 0.99%]	[0.97%, 6.77%]	[0.09%, 0.41%]	[0.00%, 0.33%]

First Interruption 0-1 Month

First Interruption 1-12 Months

* Including patients with no DAPT interruption except possible after ST through 12 months

[‡] of which 617 patients discontinued (did not restart) and 219 patients temporarily interrupted DAPT

[†] 4 of the events involved discontinuation within 1st 2 days – all probable ST (unexplained/cardiac death within 30 days). 1 event followed interruption at day 3 – definite ST at day 22.

Final thoughts

- **Second-generation DES - particularly CoCr with fluoropolymers - have low rates of ST beyond 1 month, regardless of DAPT duration**
- **All current studies and datasets are somewhat underpowered to detect very low frequency events**
- **Short DAPT duration should be considered only in patients with stable CAD**