Duration of Dual Antiplatelet Therapy
More than 6-12 Months

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Disclosures

Abbott Vascular: Advisory Board
Boston Scientific: Advisory Board

Background

- Optimal duration of DAPT after stenting has been uncertain
- CURE data suggested benefit up to 12m in ACS patients with or without stents
- Registry data suggested late stent thrombosis was a persistent problem
- Data from second generation DES studies suggest that this late ST issue may have been resolved
- Yet no large scale randomized data was available to guide decisions about long term DAPT therapy

DAPT STUDY

Dual Antiplatelet Therapy Beyond One Year After Drug-eluting Coronary Stent Procedures

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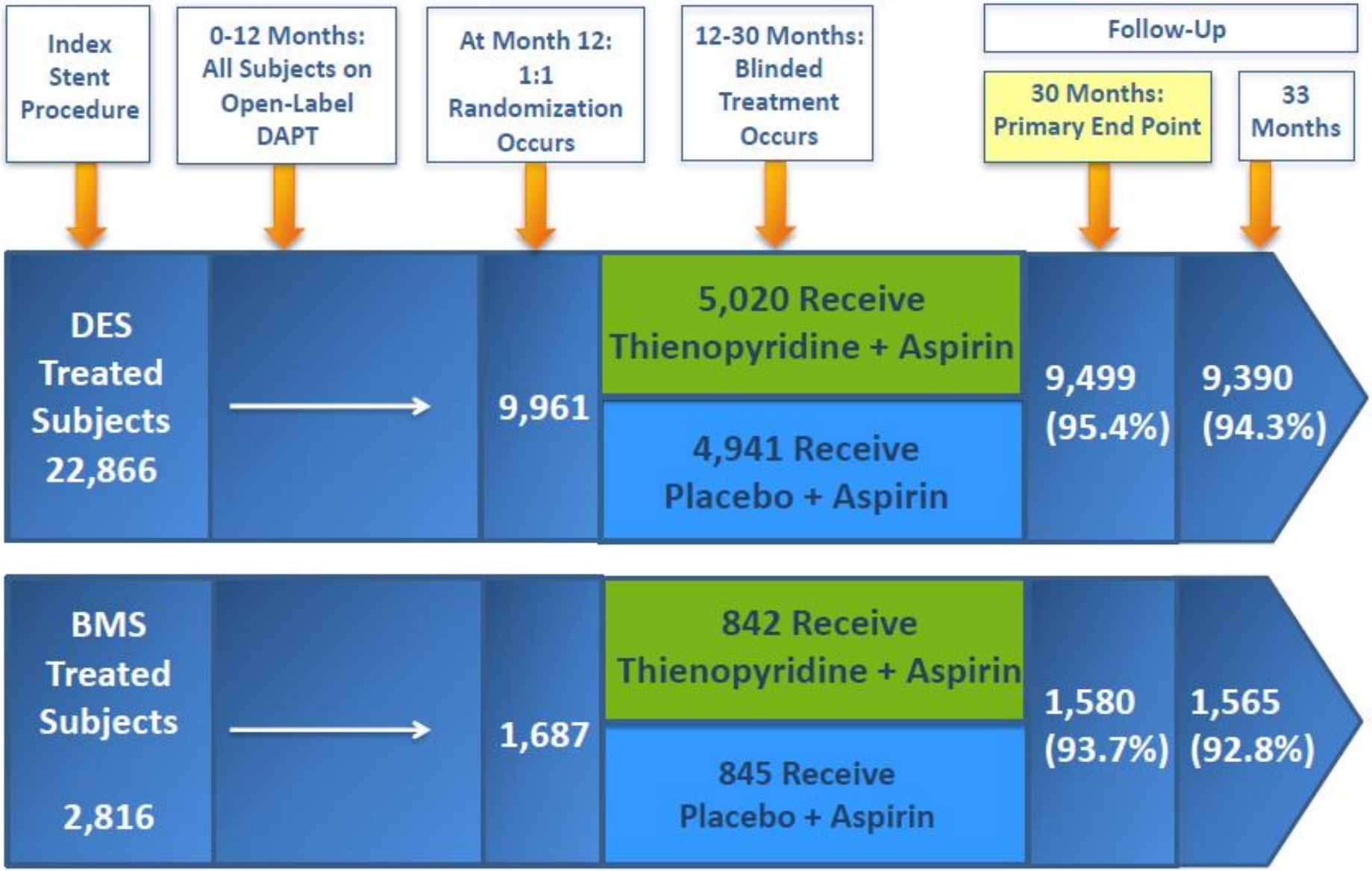
on behalf of the Dual Antiplatelet Therapy (DAPT) Study Investigators

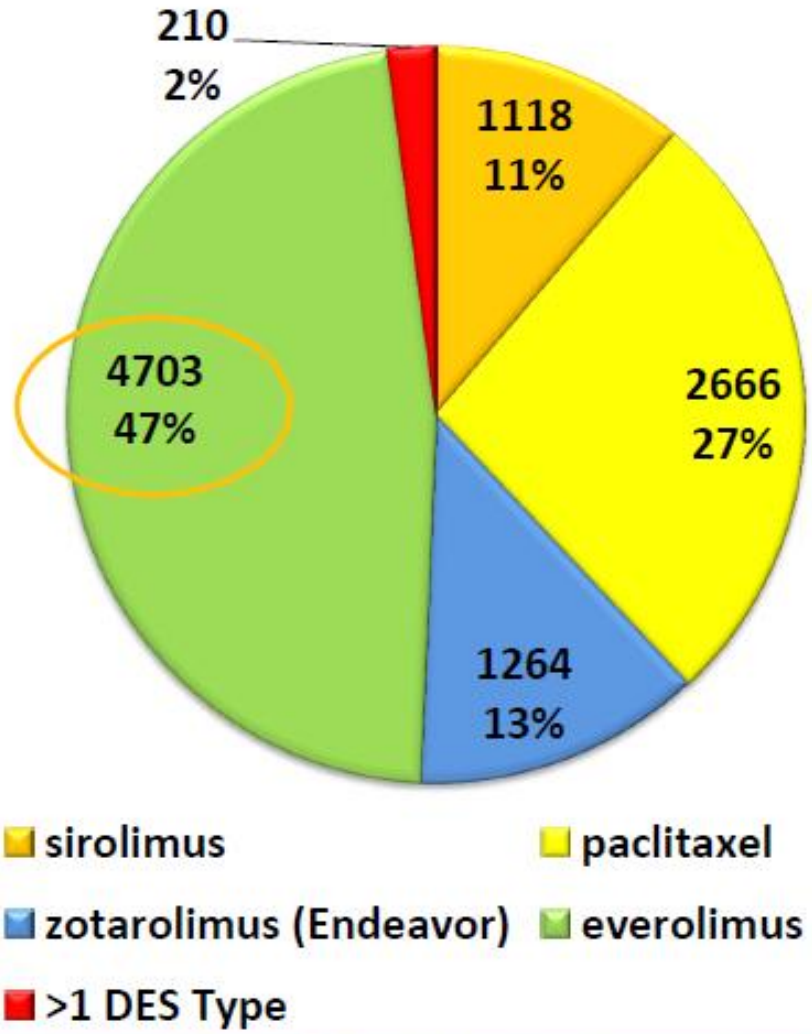
Subject Flow:
452 Sites / 11 Countries



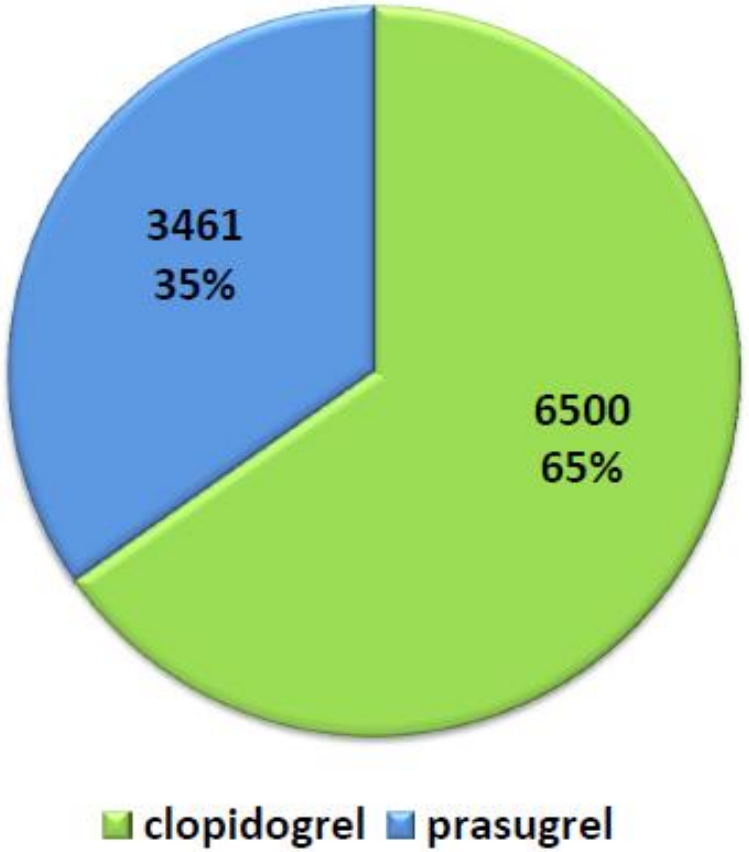
Stent & Drug Types

DAPT STUDY

Drug Eluting Stent Type

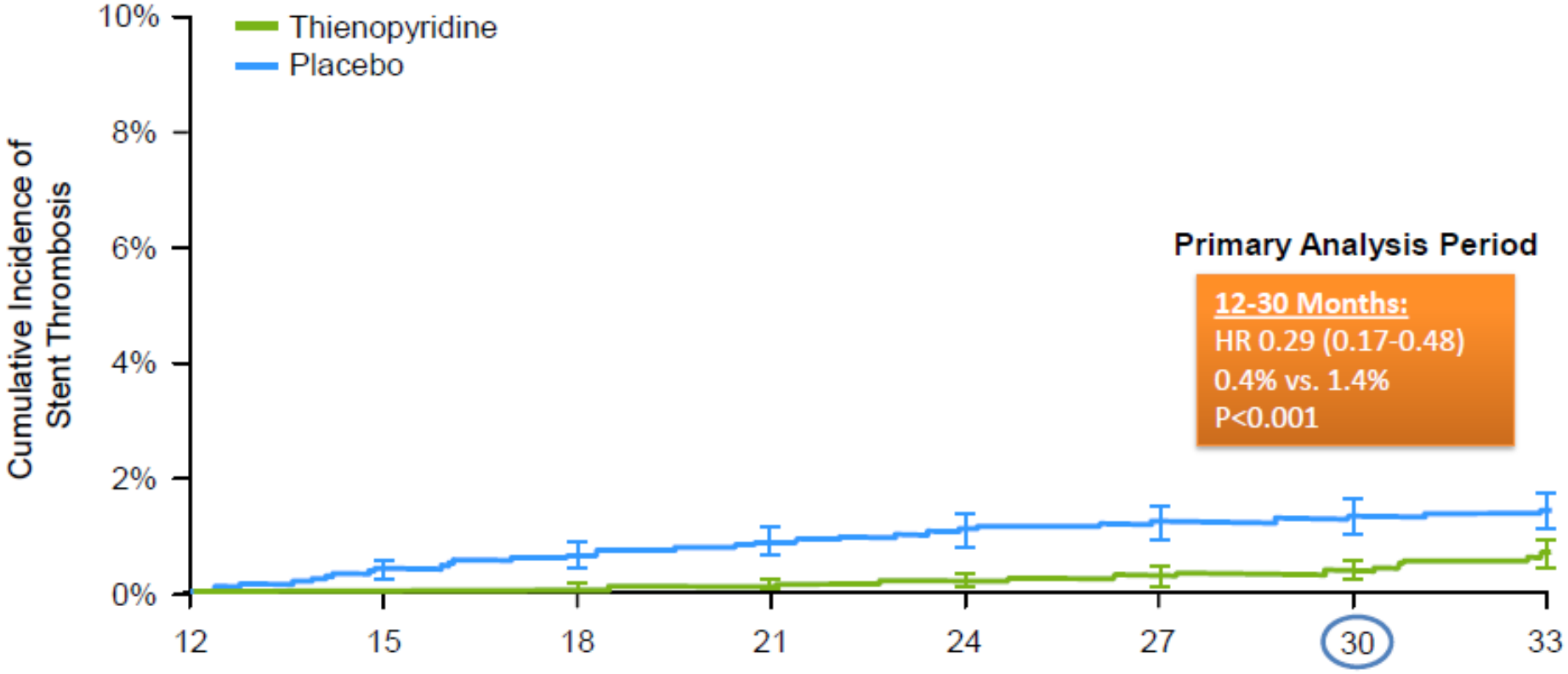


Thienopyridine Type



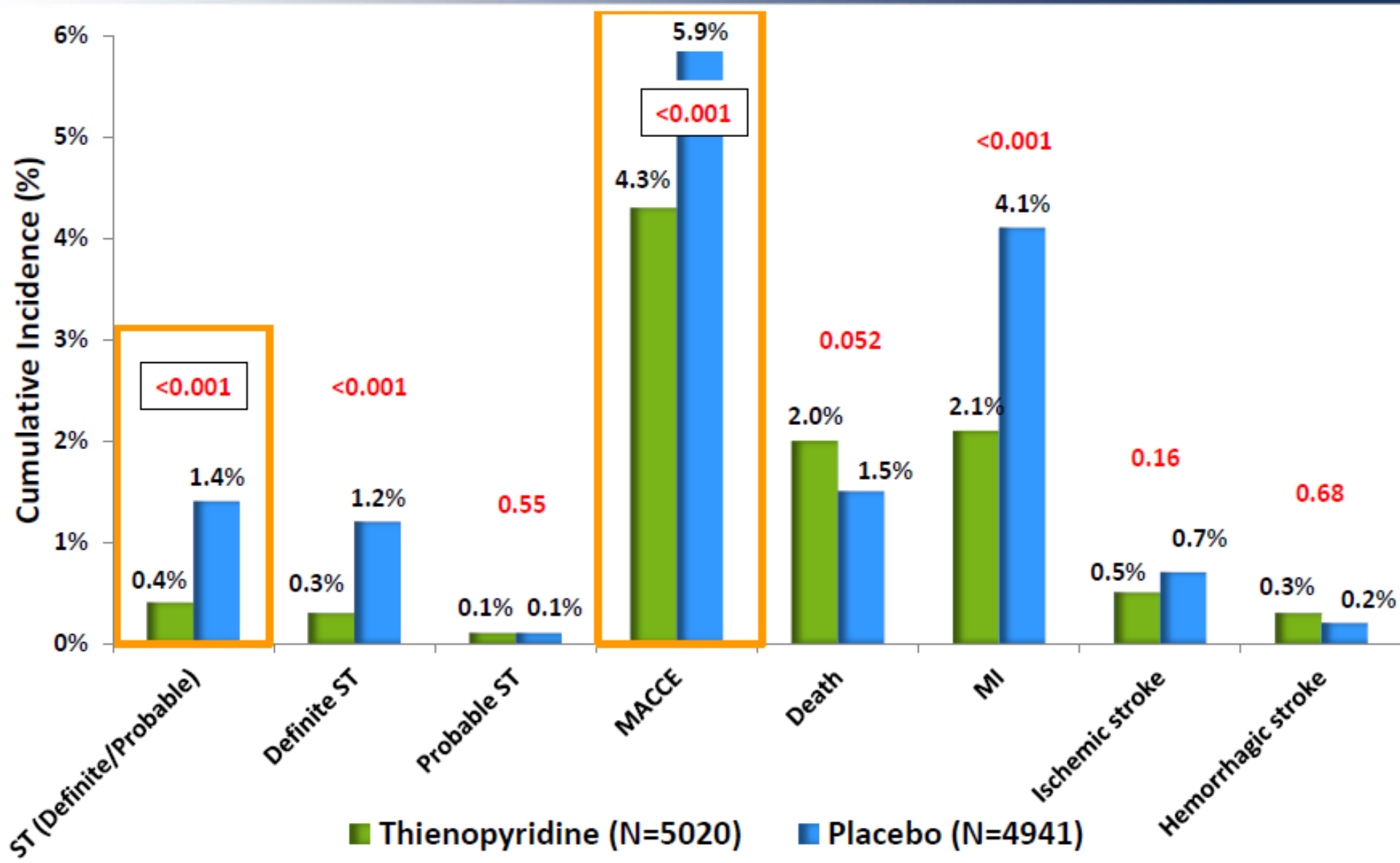
Co-Primary Effectiveness End Point
Stent Thrombosis

DAPT STUDY



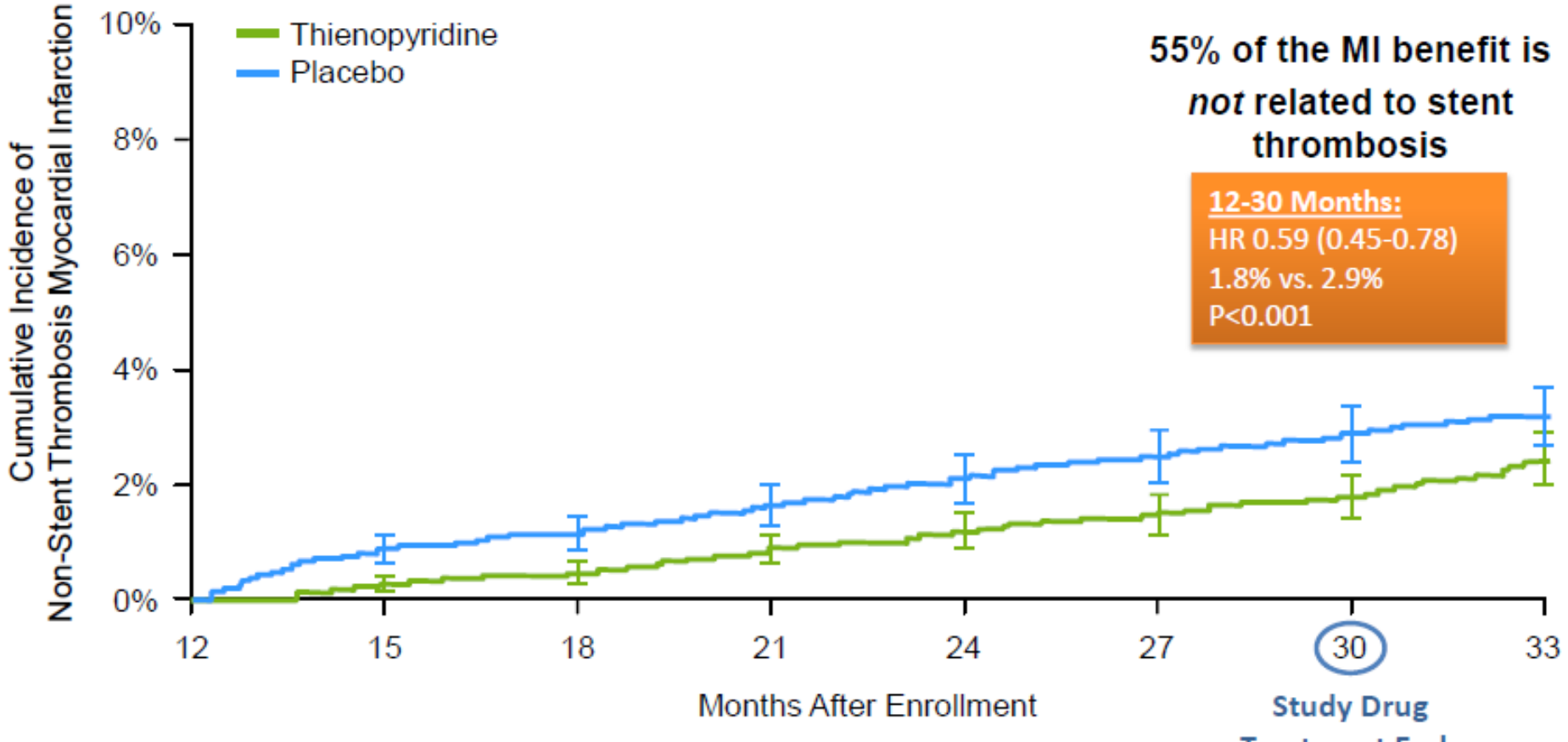
# At Risk								
Thienopyridine	5020	4934	4870	4828	4765	4686	4642	3110
Placebo	4941	4845	4775	4721	4651	4603	4556	3105

Co-Primary Effectiveness End Points & Components: 12-30 Months



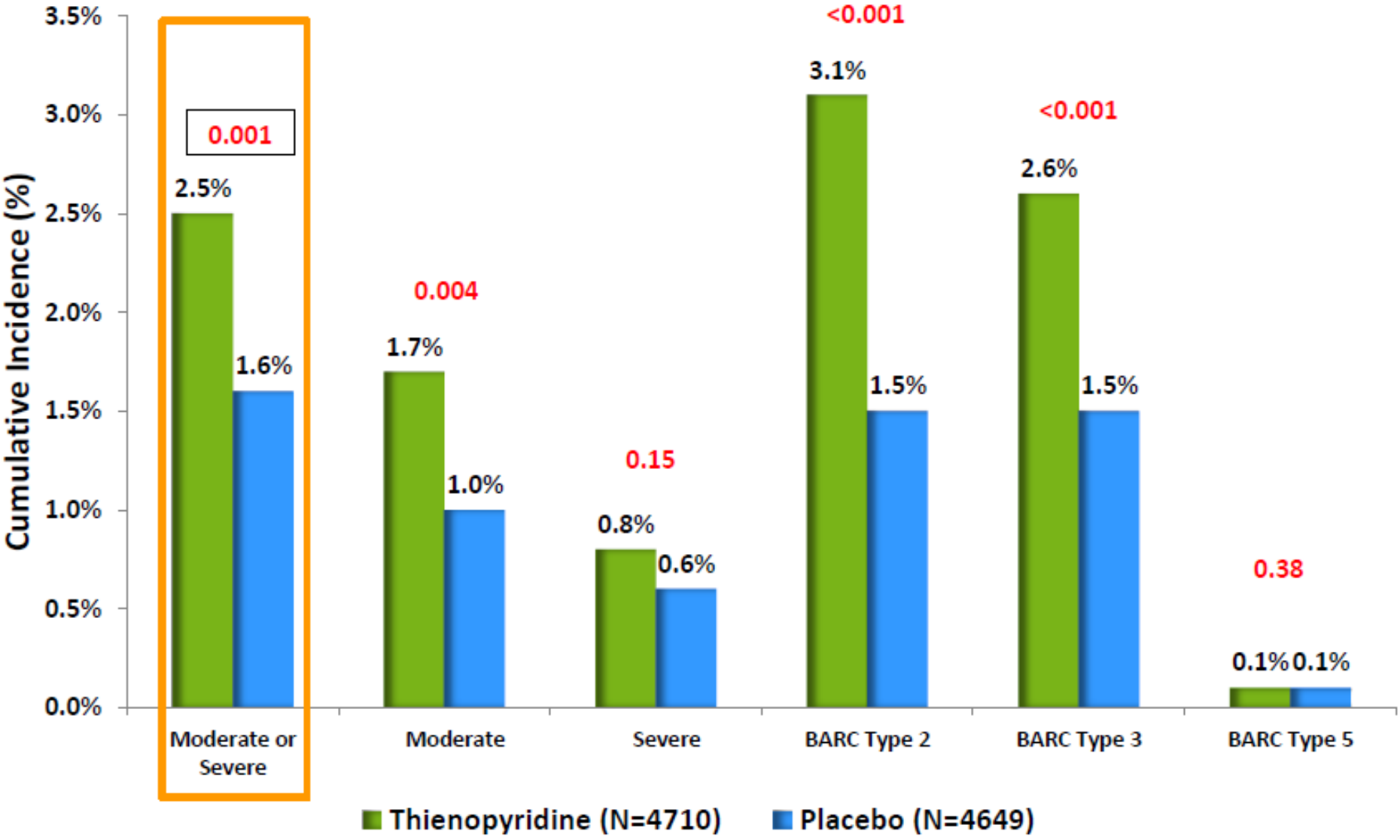
Non-Stent Thrombosis Myocardial Infarction

DAPT STUDY



# At Risk								
Thienopyridine	5020	4920	4851	4792	4721	4641	4588	3066
Placebo	4941	4820	4751	4686	4607	4547	4491	3052

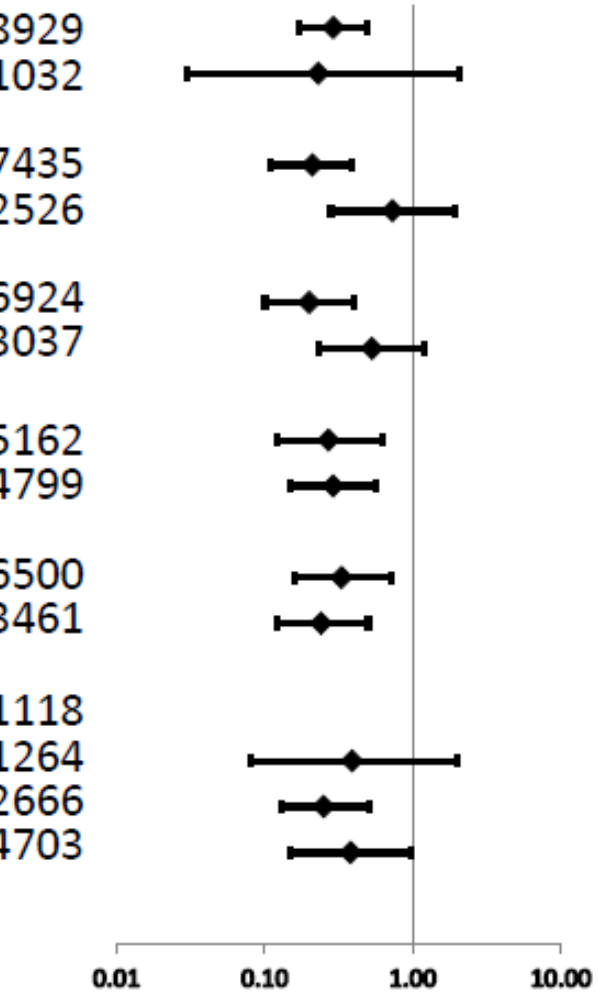
Primary Safety End Point (Moderate or Severe Bleeding): 12-30 Months



Consistency of Treatment Effect Stent Thrombosis (12-30 Months)

DAPT STUDY

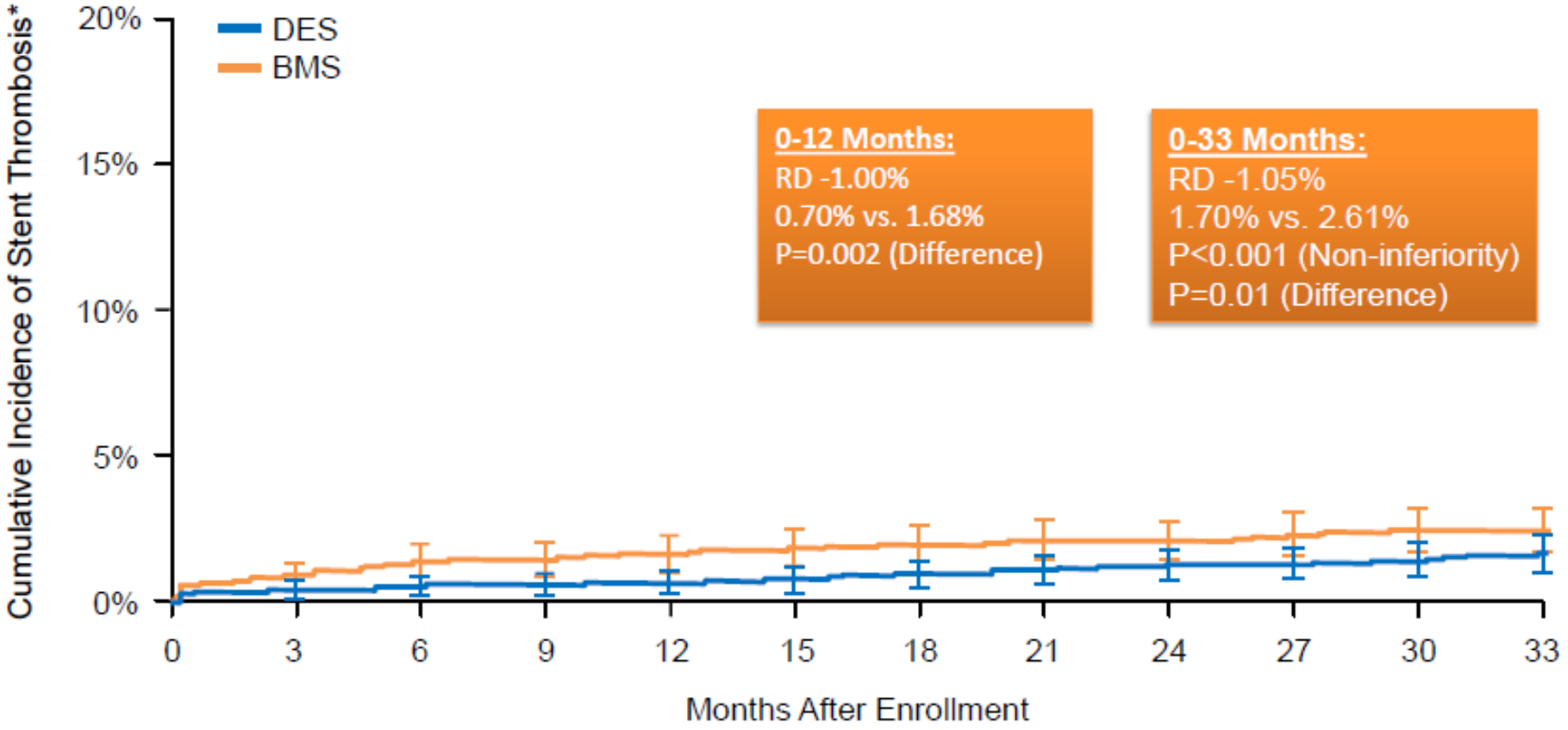
Factor	N	HR and 95% CI	Interaction P
< 75 Years	N=8929	0.29 (0.17,0.49)	0.84
>= 75 Years	N=1032	0.23 (0.03,2.06)	
Male	N=7435	0.21 (0.11,0.39)	0.04
Female	N=2526	0.73 (0.28,1.91)	
No diabetes	N=6924	0.20 (0.10,0.40)	0.08
Diabetes	N=3037	0.53 (0.23,1.20)	
No Risk Factors for ST	N=5162	0.27 (0.12,0.63)	0.89
Risk Factors for ST	N=4799	0.29 (0.15,0.56)	
Clopidogrel	N=6500	0.33 (0.16,0.71)	0.54
Prasugrel	N=3461	0.24 (0.12,0.50)	
Sirolimus	N=1118	NA*	
Zotarolimus	N=1264	0.39 (0.08,2.00)	0.76
Paclitaxel	N=2666	0.25 (0.13,0.51)	
Everolimus	N=4703	0.38 (0.15,0.97)	



*zero events in thienopyridine arm

Stent Thrombosis
Propensity-Matched DES + BMS Subjects

DAPT STUDY



No. At Risk

DES	8308	8233	8181	8125	8066	8008	7948	7896	7843	7804	7702	5013
BMS	1718	1691	1666	1648	1631	1620	1611	1598	1589	1578	1563	922

*Weighted Kaplan-Meier and risk differences (RD) are presented.

Treatment Duration by Stent Type Interaction on Stent Thrombosis/MACCE

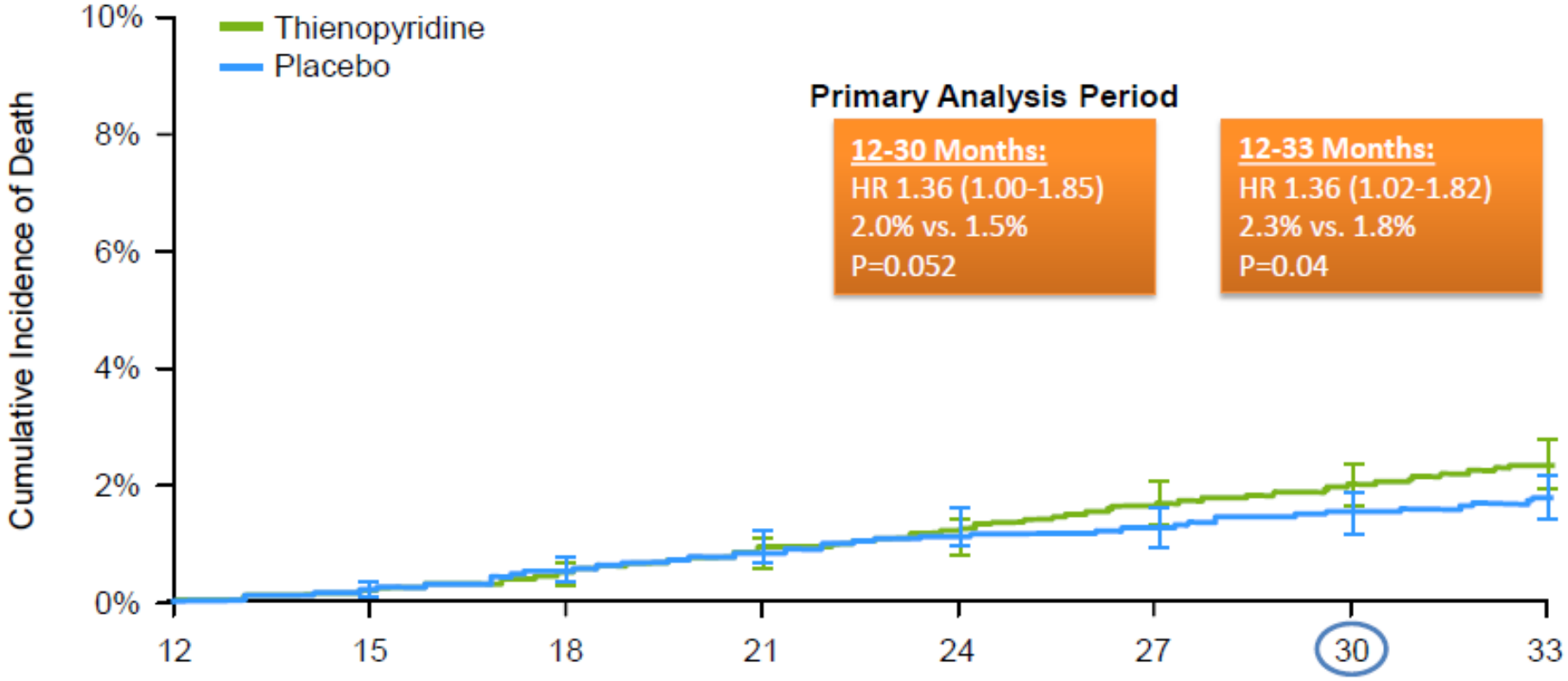
DAPT STUDY

ARC Definite/Probable ST				
Stent Type	30 Month DAPT N (%)	12 Month DAPT N (%)	HR (95% CI)	P Value Interaction
DES (N=9961)	19 (0.4%)	65 (1.4%)	0.29 (0.17-0.48)	0.42
BMS (N=1687)	4 (0.5%)	9 (1.1%)	0.49 (0.15-1.65)	

MACCE				
Stent Type	30 Month DAPT N (%)	12 Month DAPT N (%)	HR (95% CI)	P Value Interaction
DES (N=9961)	211 (4.3%)	285 (5.9%)	0.71 (0.59-0.85)	0.32
BMS (N=1687)	33 (4.0%)	38 (4.7%)	0.92 (0.57-1.47)	

All-Cause Mortality

DAPT STUDY



Primary Analysis Period

12-30 Months:
HR 1.36 (1.00-1.85)
2.0% vs. 1.5%
P=0.052

12-33 Months:
HR 1.36 (1.02-1.82)
2.3% vs. 1.8%
P=0.04

# At Risk								
Thienopyridine	5020	4936	4875	4835	4777	4703	4663	3139
Placebo	4941	4866	4805	4761	4700	4659	4618	3159

All-Cause Mortality

DAPT STUDY

	12-30 Months			
	Thienopyridine N=5020	Placebo N=4941	P-Value	Absolute Difference
All-Cause Mortality	**98 (2.0%)**	**74 (1.5%)**	**0.052**	**24 (0.5%)**
Cardiac	45 (0.9%)	47 (1.0%)	0.98	-2 (-0.1%)
Vascular	5 (0.1%)	5 (0.1%)	0.98	0 (-)
Non-Cardiovascular	48 (1.0%)	22 (0.5%)	0.002	26 (0.5%)

Cumulative incidence is presented according to Kaplan-Meier method

Additional Adjudication and Analysis

DAPT STUDY

Non-Cardiovascular Deaths, 12-33 Months			
Relatedness for Deaths*	Thienopyridine N=5020	Placebo N=4941	P-value
Bleeding-Related Death	11 (0.22%)	3 (0.06%)	0.057
Trauma-Related Death	9 (0.18%)	2 (0.04%)	0.07
Cancer-Related Death	31 (0.62%)	14 (0.28%)	0.02

*overlapping categories/not mutually exclusive

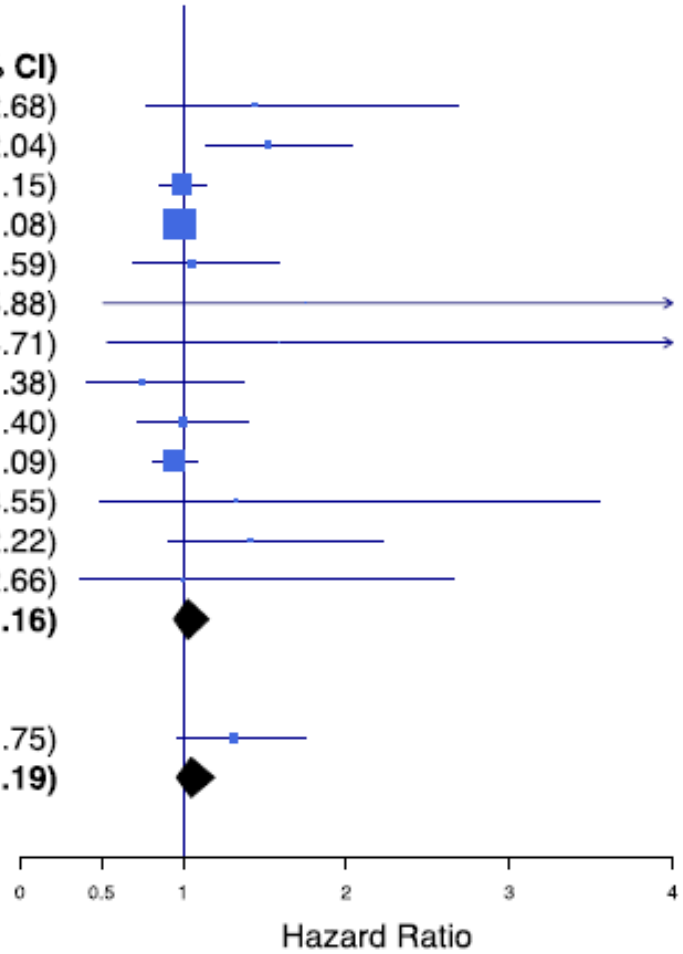
Nine (7 vs. 2) of the 11 trauma-related deaths were also bleeding-related.
Three (3 vs. 0) of the 45 cancer-related deaths were also bleeding-related.

Site-Reported Cancer Incidence, 12-33 Months			
	Thienopyridine	Placebo	P-value
Cancer reported after randomization	102 (2.03%)	80 (1.62%)	0.14

Randomized Trials of Thienopyridine+Aspirin vs. Aspirin Alone; All-Cause Mortality

DAPT STUDY

Study	Study Arm N (# Events)	Control Arm N (# Events)	HR (95% CI)
CASPAR	425(24)	426(17)	1.44 (0.77, 2.68)
SPS3	1503(113)	1517(77)	1.52 (1.14, 2.04)
CHARISMA	7802(371)	7801(374)	0.99 (0.86, 1.15)
ACTIVE	3772(825)	3782(841)	0.98 (0.89, 1.08)
OPTIMIZE	1556(45)	1553(43)	1.05 (0.69, 1.59)
EXCELLENT	721(7)	722(4)	1.75 (0.51, 5.88)
RESET	1058(8)	997(5)	1.59 (0.54, 4.71)
CREDO	1053(18)	1063(24)	0.75 (0.41, 1.38)
PRODIGY	987(65)	983(65)	1.00 (0.72, 1.40)
CURE	6259(369)	6303(390)	0.95 (0.82, 1.09)
ARCTIC–Interruption	635(7)	624(9)	1.32 (0.49, 3.55)
DES LATE	2531(46)	2514(32)	1.41 (0.91, 2.22)
SECURITY	717(8)	682(8)	1.00 (0.38, 2.66)
Overall(DAPT NOT Included)	**29019(1906)**	**28967(1889)**	**1.03 (0.94, 1.16)**
Q = 14.87, p = 0.25; I2 = 12.6%			
DAPT	5862(106)	5786(84)	1.31 (0.97, 1.75)
Overall(DAPT Included)	**34881(2012)**	**34753(1973)**	**1.05 (0.96, 1.19)**
Q = 17.68, p = 0.17; I2 = 26.5%			



Total N=69644, ~139000 pt yrs)

Elmariah S, Mauri L, Doros G, O'Neill KE, Steg PG, Kereiakes DJ, Yeh RW. Extended Duration Dual Antiplatelet Therapy and Mortality: A Systematic Review and Meta-analysis. *The Lancet*. Online ahead of print November 16, 2014.

Conclusions

- The DAPT study demonstrates continued benefit through reduction in ST and MACE from 12m-30m
- The benefit was consistent through all subgroups
  - True for BMS as well as DES
  - True for non-ACS as well as ACS
- Longer DAPT was associated with increased bleeding but bleeding was not associated with mortality

Conclusions

- Higher mortality seen in the DAPT arm was likely related to play of chance but prolonged DAPT certainly does not appear to lower mortality
  - Likely related to small absolute event numbers which brings into question the clinical relevance of the benefit of prolonged DAPT

Conclusions

- **So what are the clinical implications of the landmark study?**
- There is benefit to prolonged DAPT (possibly indefinitely)
- But the absolute benefit is small and does not reduce mortality
- Patients who tolerate DAPT without bleeding should probably continue DAPT for at least 30m if not indefinitely but for those that cannot tolerate or do not want to continue prolonged DAPT the penalty in terms of adverse outcomes is small