

Ticagrelor With Asplrin or ALone In HiGH-Risk Patients After Coronary InTervention for Acute Coronary Syndrome

**TWILIGHT-ACS** 

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# **Disclosures**

Affiliation/Financial Relationship	Company
Advisory board/personal fees	Amgen; AstraZeneca; Boston Scientific
Research Funding to Institution	AstraZeneca

# Background

- The prevailing construct of dual antiplatelet therapy (DAPT) as the preferred treatment for patients with acute coronary syndromes (ACS) originated from clinical trials showing that the addition of an oral P2Y<sub>12</sub> inhibitor to aspirin significantly lowers recurrent ischemic events as compared with aspirin alone.<sup>1,2</sup>
- The benefits, or harms, of maintaining aspirin as a long-term component of DAPT in the setting of ACS remains unknown, however, as aspirin served as a background agent in earlier studies.
- Recent studies have suggested that aspirin-free strategies lower bleeding without increasing ischemic risk as compared with conventional DAPT in select patients undergoing percutaneous coronary intervention (PCI).<sup>3,4,5</sup>

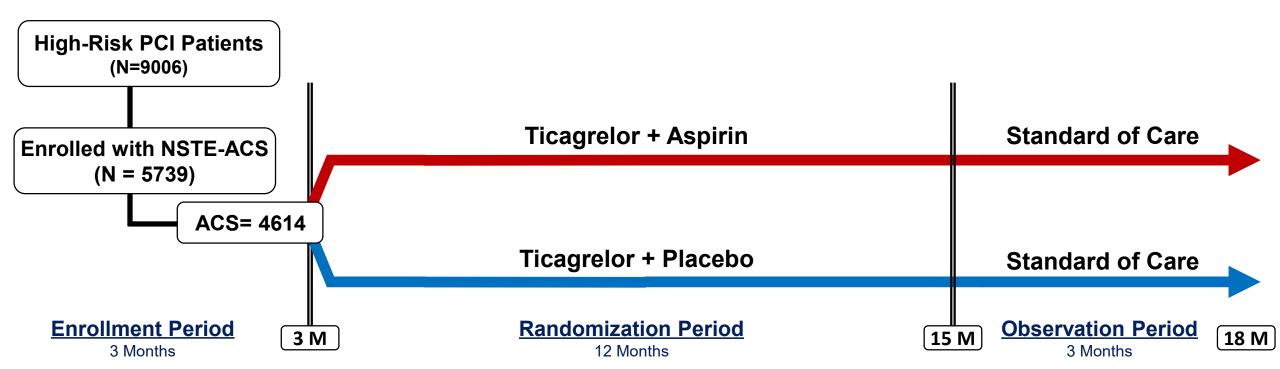
<sup>1</sup>Mehta et al., Lancet 2001; <sup>2</sup>Levine et al., JACC 2016; <sup>3</sup>Mehran et al., NEJM 2019; <sup>4</sup>Watanabe et al., JAMA 2019; <sup>5</sup>Hahn et al., JAMA 2019

# Study Objective

To examine the effect of antiplatelet monotherapy with ticagrelor alone versus ticagrelor plus aspirin among patients with non-ST elevation acute coronary syndromes (NSTE-ACS) undergoing PCI with drug eluting stents who had already completed a 3-month course of DAPT

# Study Design

- Randomized, double-blind placebo controlled trial in 187 sites and 11 countries
- High-risk patients underwent PCI and were treated with ticagrelor plus aspirin for 3 months
- Event-free and adherent patients were randomized to aspirin versus placebo and continued ticagrelor for an additional year



### Inclusion/Exclusion Criteria

#### Must meet at least one clinical AND one angiographic criterion

#### **Clinical criteria**

Age ≥65 years

Female gender

Troponin positive ACS

Established vascular disease (previous MI, documented PAD or CAD/PAD revasc)

DM treated with medications or insulin

CKD (eGFR <60ml/min/1.73m<sup>2</sup> or CrCl <60ml/min)

#### **Angiographic criteria**

Multivessel CAD

Target lesion requiring total stent length >30mm

Thrombotic target lesion

Bifurcation lesion(s) with Medina X,1,1 classification requiring ≥2 stents

Left main (≥50%) or proximal LAD (≥70%) lesions

Calcified target lesion(s) requiring atherectomy

**Key Exclusions:** STEMI; Salvage PCI; need for chronic oral anticoagulation; planned coronary revascularization

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### **TWILIGHT-ACS: Methods**

#### **Target Population**

Randomized TWILIGHT participants presenting with unstable angina or non-ST elevation MI (NSTE-ACS)

#### **Endpoints**

*Primary*: BARC 2, 3 or 5 bleeding between 0 - 12 months after randomization *Secondary*: Non-fatal MI, stroke or all-cause death between 0 - 12 months after randomization

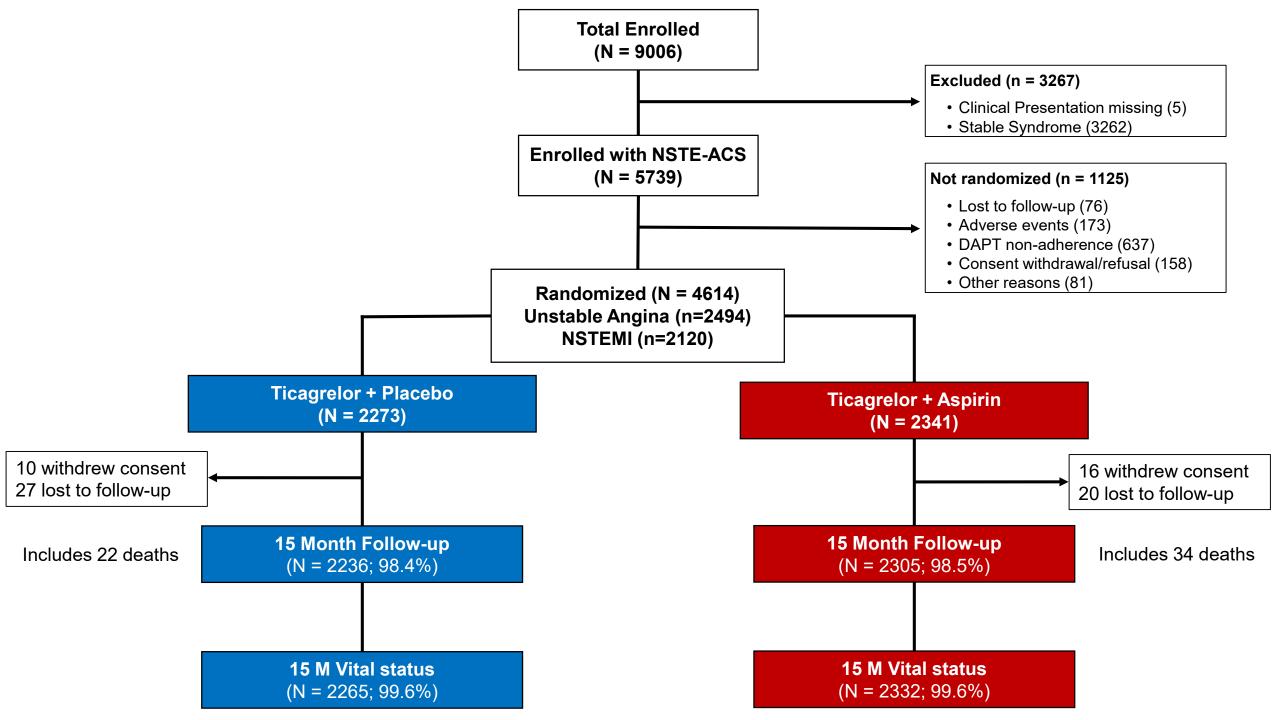
#### **Analytic Approach**

Survival analyses using the Kaplan-Meier method

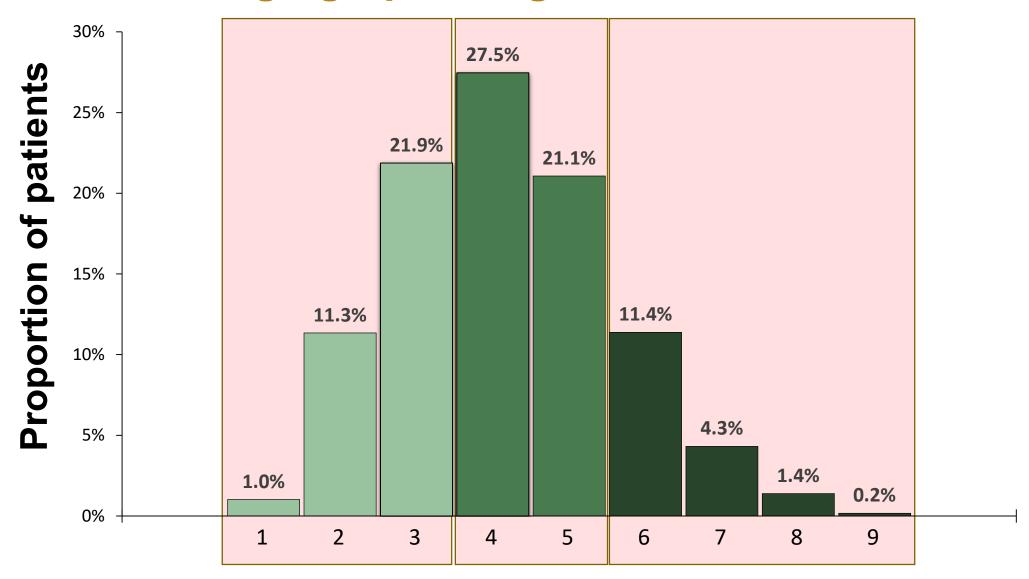
Hazard ratios and 95% confidence intervals (CI) generated using Cox regression

Treatment effect examined in relation to number of clinical and angiographic risk factors

Stratified analyses among those with unstable angina or NSTEMI



# TWILIGHT-ACS: Distribution of Pre-Specified Clinical and Angiographic High-Risk Features



**Number of Clinical and Angiographic High-Risk Features** 

### **TWILIGHT-ACS: Patient Characteristics**

### **Baseline Demographics**

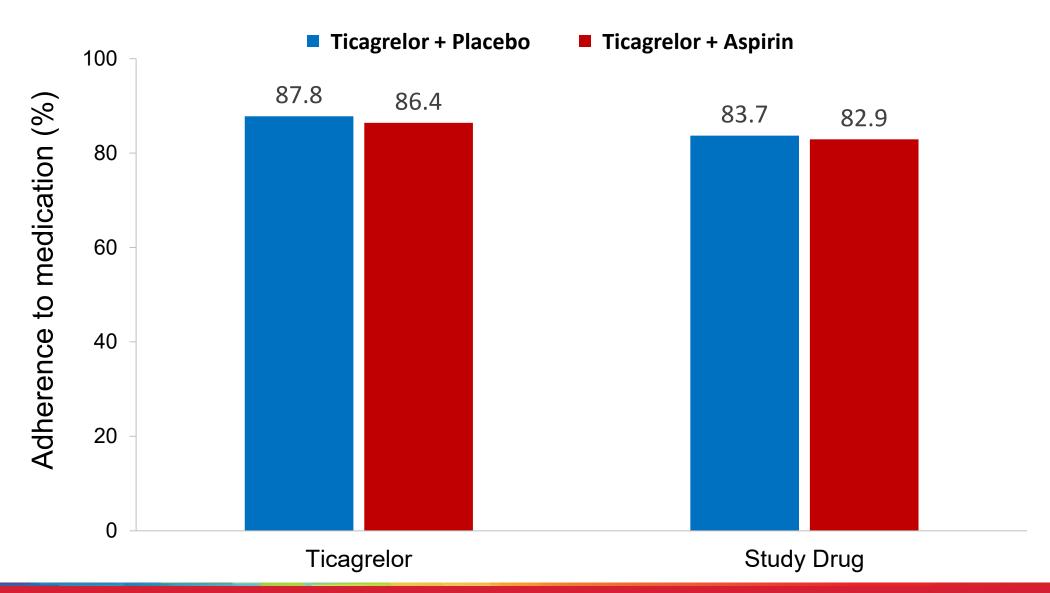
Variable	Tica + Placebo (n=2273)	Tica + Aspirin (n=2341)	p-value
Age, years [Mean ± SD]	$64.2 \pm 10.5$	64.2 ± 10.6	0.99
Female sex	25.5%	24.8%	0.56
Age, years [Mean ± SD]	64.2 ± 10.5	64.2 ± 10.6	0.99
Diabetes Mellitus	35.6%	34.3%	0.36
Current Smoker	23.3%	26.6%	0.02
Previous MI	25.4%	25.2%	0.83
Anemia	19.9%	19.5%	0.76
<b>Current Smoker</b>	23.3%	26.6%	0.02
Previous MI	25.4%	25.2%	0.83
Previous PCI	34.2%	34.4%	0.91
Previous CABG	8.8%	8.5%	0.68

### **TWILIGHT-ACS: Patient Characteristics**

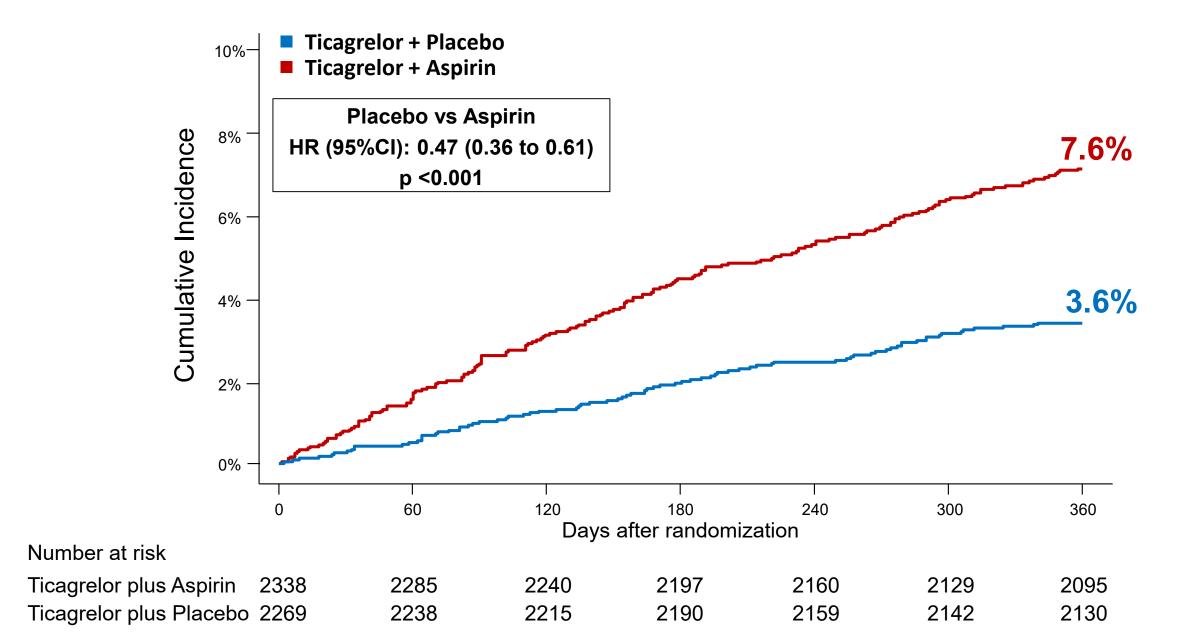
#### **Procedural Details**

Variable	Tica + Placebo (n=2273)	Tica + Aspirin (n=2341)	p-value
Radial access	76.7%	76.3%	0.78
Multivessel CAD	61.9%	59.5%	0.08
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esion morphology			
Thrombus	14.9%	15.4%	0.60
Calcification (Moderate/Severe)	12.0%	11.9%	0.92
otal stent length	40.5 ± 24.5	39.8 ± 24.6	0.35
Calcification (Moderate/Severe)	12.0%	11.9%	0.92
Any bifurcation	12.5%	12.6%	0.98
Chronic total occlusion	5.6%	6.1%	0.49
Total stent length	40.5 ± 24.5	39.8 ± 24.6	0.35

### **TWILIGHT-ACS: Adherence by Treatment Allocation**



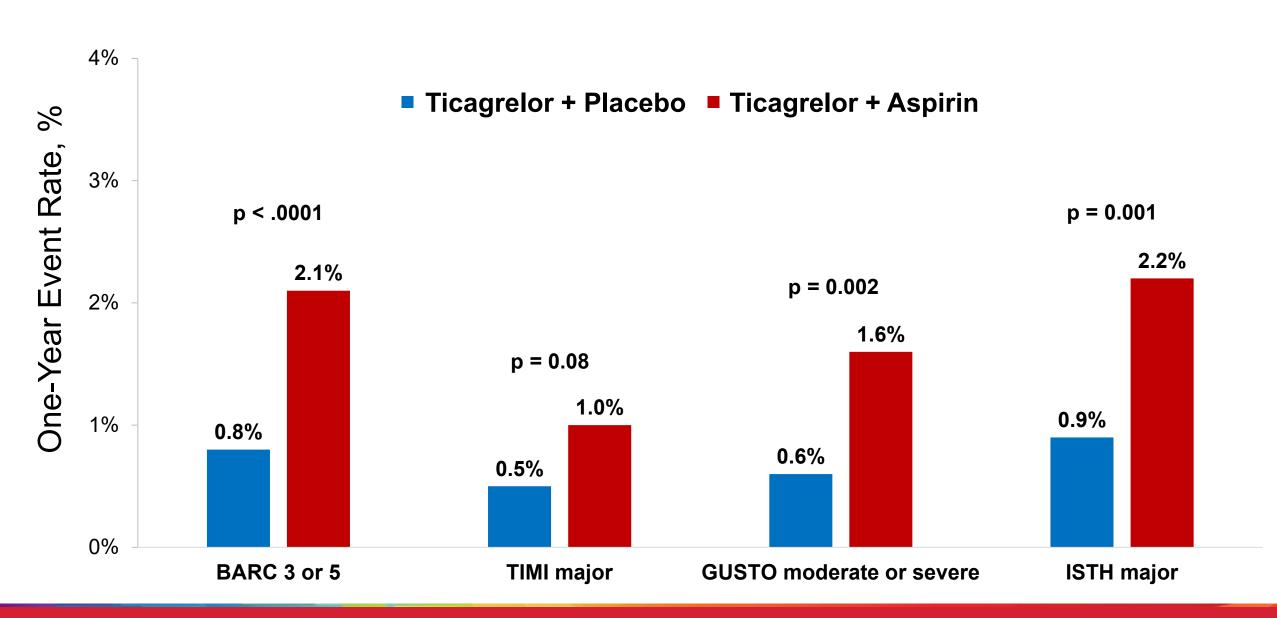
## TWILIGHT-ACS: BARC 2, 3 or 5



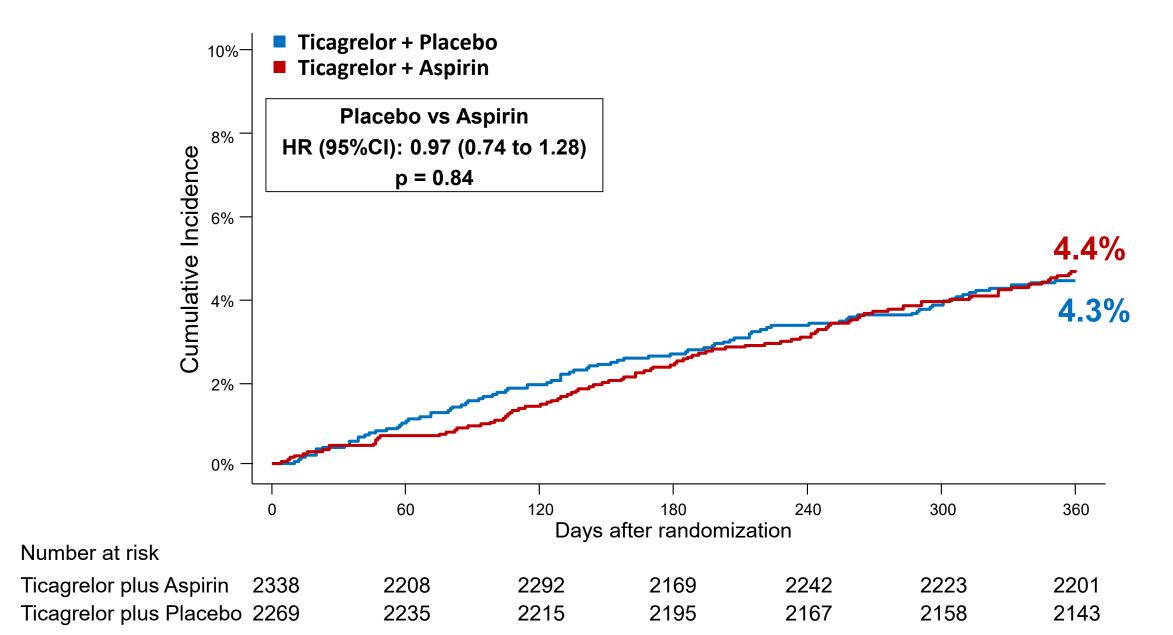
### TWILIGHT-ACS: BARC 2, 3 or 5 in Relation to Risk Factor Burden

Number of Risk	One-yea	r rate (%)		Hazard ratio (95% CI)	
Factors	T+P	T+A		1102010 1010 (0070 01)	
1 – 3 (n=1579)	3.5%	7.0%	<b>—</b>	0.49 (0.31-0.77)	
4, 5 (n=2239)	3.7%	7.3%		0.50 (0.34-0.72)	p <sub>int</sub> = 0.69
6 – 9 (n=796)	3.6%	9.4% -	•	0.37 (0.20-0.68)	
	0.1	1		1	1

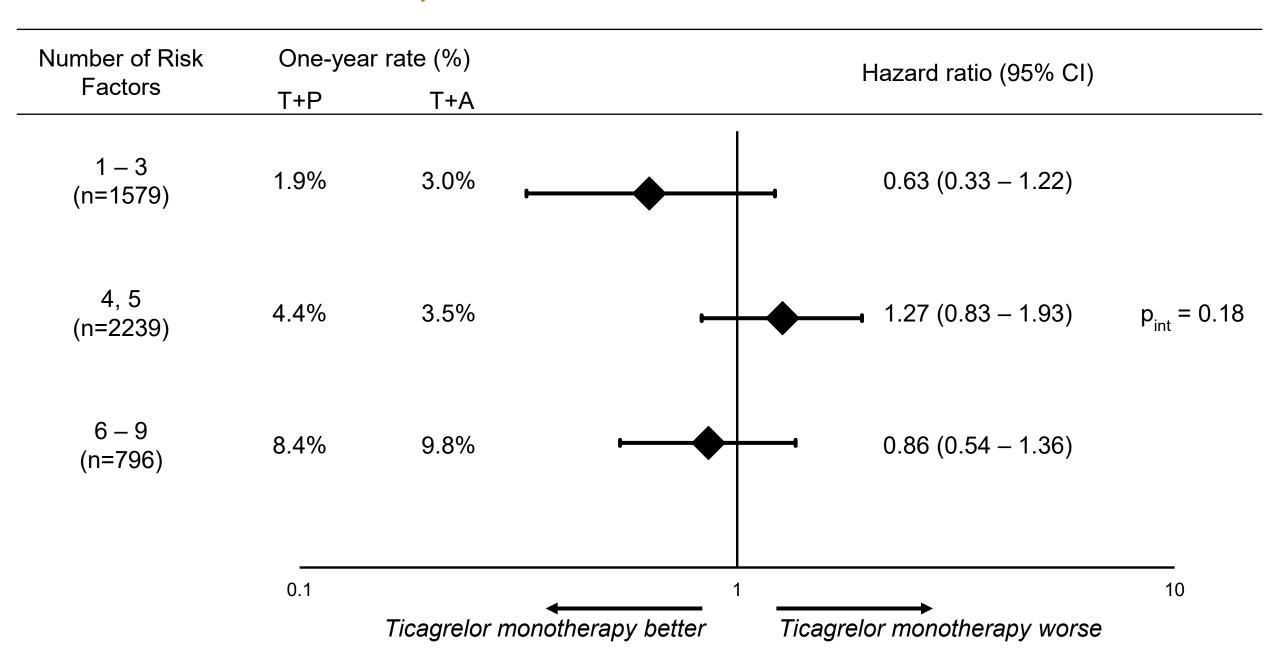
# **TWILIGHT-ACS: Pre-Specified Bleeding Endpoints**



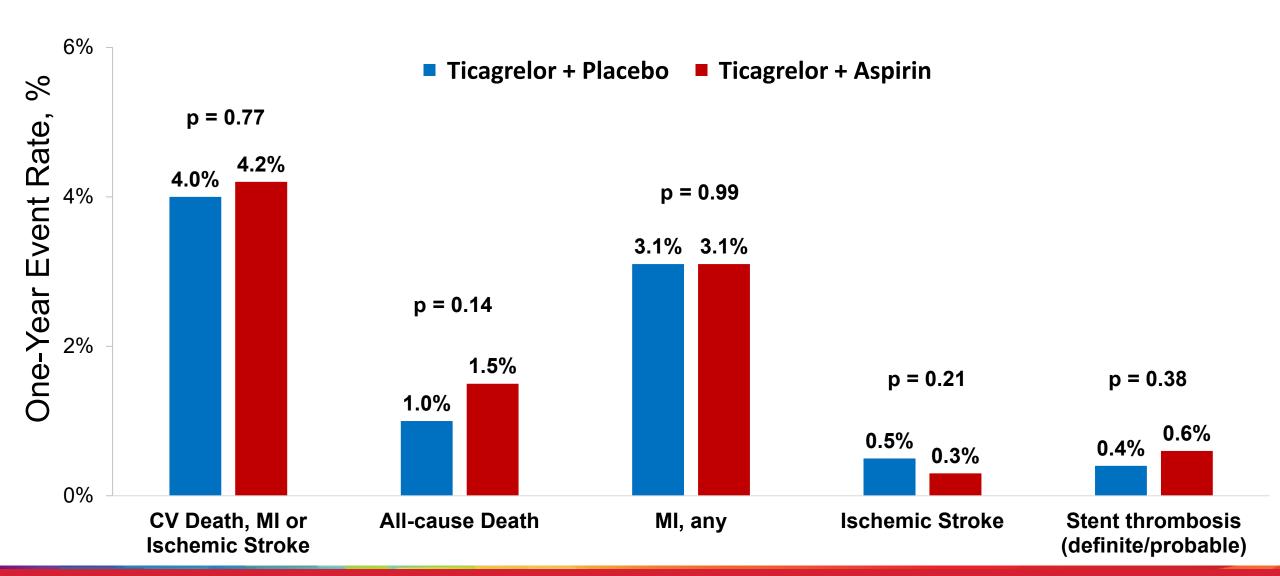
## TWILIGHT-ACS: Death, MI or Stroke



#### TWILIGHT-ACS: Death, MI or Stroke in Relation to Risk Factor Burden



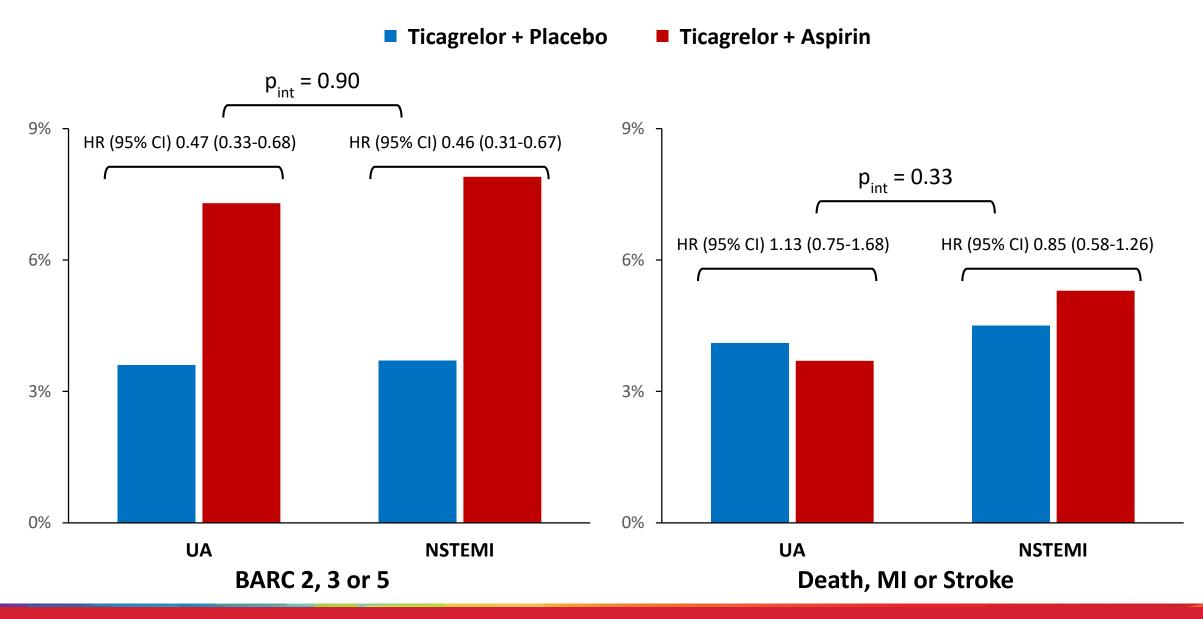
# **TWILIGHT-ACS: Pre-specified Ischemic Endpoints**



### TWILIGHT-ACS: Adjusted Hazards for Death, MI, Stroke

Variable	HR (95% CI)
Ticagrelor plus Placebo	1.02 (0.74-1.41)
Age, per year increase	1.01 (0.99-1.03)
Female sex	0.92 (0.62-1.36)
Troponin (+)	1 77 (1 23-2 55)
Troponin (+)	1.77 (1.23-2.55)
Established vascular disease	2.77 (1.94-3.97)
Atherectomy use	2.46 (1.19-5.1)
BARC type 3 or 5 Bleeding (time-updated covariate)	6.7 (3.1-14.6)
Bifurcation requiring 2 stents	1.32 (0.61-2.83)
Atherectomy use	2.46 (1.19-5.1)
Thrombotic lesion	1.09 (0.67-1.77)
Left main or LAD lesion	0.90 (0.61-1.34)
BARC type 3 or 5 Bleeding (time-updated covariate)	6.7 (3.1-14.6)

### TWILIGHT-ACS: Stratified Analysis According to UA or NSTEMI



# Limitations

- Extrapolating results to STEMI patients not possible given trial design.
- Generalizing to broader population of PCI patients without high-risk features pre-specified in TWILIGHT is limited.
- Use of ticagrelor as background antiplatelet agent thereby precluding inference for other P2Y<sub>12</sub> inhibitors.
- Lack of power to detect differences in the risk of important yet rare clinical events, such as stent thrombosis and stroke.

# Conclusions

- Among patients with NSTE-ACS undergoing PCI with DES and who have completed
  a 3-month course of DAPT with ticagrelor plus aspirin, continued treatment with
  ticagrelor alone significantly lowers clinically relevant and major bleeding without
  increasing risk for ischemic events over one year.
- The effect of ticagrelor monotherapy with respect to bleeding and ischemic events is uniform across different levels of risk.
- Results are unchanged for patients presenting with UA or NSTEMI.
- Overall findings are concordant with the results of the primary trial.

# Acknowledgement

We thank all country leaders, investigators, coordinators and study participants who made *TWILIGHT* possible!

# Thank you!

