

# **Supplemental Material**

**Table S1. Baseline characteristics in the overall population stratified by high and low bleeding risk.**

<b>Characteristic</b>	<b>High Bleeding Risk N=4,054 N (%)</b>	<b>Low Bleeding Risk N=16,888 N (%)</b>	<b>p-value</b>
Age $\geq$ 75	986 (24.3)	2051 (12.1)	<0.001
Female	813 (20.1)	4190 (24.8)	<0.001
BMI, median (IQR)	27.1 (24.2 – 30.4)	28.1 (25.4 – 31.2)	<0.001
Current Smoking	485 (12.0)	3019 (17.9)	<0.001
COPD	318 (7.9)	1150 (6.8)	0.0203
History of Hypertension	3218 (79.4)	13020 (77.1)	0.0018
Hypercholesterolemia	3061 (75.5)	13019 (77.1)	0.0309
eGFR < 60 ml/min	1422 (35.3)	3366 (20.2)	<0.001
Diabetes Mellitus	1616 (39.9)	5119 (30.3)	<0.001
Peripheral Artery Disease	295 (7.3)	835 (4.9)	<0.001
Multivessel Coronary Disease	2333 (57.6)	10090 (59.8)	0.0109
History of PCI	3295 (81.3)	14084 (83.4)	0.0012
History of CABG	239 (5.9)	723 (4.3)	<0.001

**Table S2. Primary endpoint and TIMI major bleeding rates stratified by high versus low bleeding and ischemic risk.**

		<b>High Bleeding Risk events (KM%)</b>	<b>Low Bleeding Risk events (KM%)</b>
<b>High Ischemic Risk</b>	<b><i>PEP</i></b>	N= 3511 353 (11.36%)	N= 14106 1055 (8.29%)
	<b><i>TMB</i></b>	N= 3511 127 (5.25%)	N= 14106 266 (2.61%)
<b>Low Ischemic Risk</b>	<b><i>PEP</i></b>	N= 542 22 (4.39%)	N=2778 113 (4.58%)
	<b><i>TMB</i></b>	N= 542 10 (2.57%)	N=2778 29 (1.40%)

*\*High ischemic risk defined as age  $\geq$  75, hypertension and current smoking, low ischemic risk is defined as the age  $<$  75, no hypertension and no current smoking.*

(NOTE: A total of 20937 subjects out of safety population were included in this analysis. There were five subjects with missing Ischemic risk status.)

(NOTE: 3 year KM estimates are reported)

(NOTE: PEP = CVD/MI/Stroke. TMB = TIMI Major or minor bleeding)

**Table S3: Other outcomes of ticagrelor 60 mg vs. placebo stratified by high or low bleeding risk at baseline.**

Endpoint	Ticagrelor 60 mg n (KM %)	Placebo n (KM %)	HR 95% CI	P for interaction
<b>Myocardial infarction</b>				
Lower bleeding risk	227 (4.39)	264 (5.09)	0.85 (0.72-1.02)	0.71
Higher bleeding risk	58 (5.14)	74 (5.94)	0.80 (0.56-1.12)	
<b>Stroke</b>				
Lower bleeding risk	67 (1.38)	100 (1.96)	0.66 (0.49-0.91)	0.12
Higher bleeding risk	24 (1.85)	22 (1.85)	1.12 (0.63-1.99)	
<b>Coronary heart disease death</b>				
Lower bleeding risk	61 (1.25)	97 (1.90)	0.63 (0.45-0.86)	0.008
Higher bleeding risk	45 (3.70)	35 (2.85)	1.30 (0.84-2.03)	
<b>Non-CV Death</b>				
Lower bleeding risk	74 (1.44)	73 (1.44)	1.01 (0.73-1.39)	0.88
Higher bleeding risk	39 (3.82)	38 (3.09)	1.06 (0.68-1.66)	
<b>ICH or fatal bleeding</b>				
Lower bleeding risk	22 (0.60)	22 (0.54)	1.09 (0.60-1.97)	0.56
Higher bleeding risk	11 (1.25)	8 (0.91)	1.51 (0.61-3.75)	
<b>Myocardial infarction, Stroke, death, or TIMI major bleeding</b>				
Lower bleeding risk	477 (11.36)	531 (11.51)	0.97 (0.86 – 1.10)	0.18
Higher bleeding risk	181 (18.67)	170 (15.50)	1.15 (0.93 – 1.42)	
<b>Myocardial infarction, Stroke, death, or TIMI major or minor bleeding</b>				
Lower bleeding risk	513 (9.99)	546 (10.51)	0.94 (0.83 – 1.06)	0.0697
Higher bleeding risk	201 (17.02)	177 (14.15)	1.16 (0.95 – 1.43)	

HR=Hazard Ratio, CI=Confidence Interval, CV= Cardiovascular, ICH= Intracranial Hemorrhage, KM= Kaplan Meier

**Table S4. PRECISE-DAPT score versus PEGASUS low or high bleeding risk, based on anemia and history of spontaneous bleeding.**

PRECISE-DAPT Score	PEGASUS TIMI 54 Low bleeding risk*		PEGASUS TIMI 54 High bleeding risk*	
	N (%)	ARI** 3 yrs KM rate (%)	N (%)	ARI** 3 yrs KM rate (%)
<b>Very low risk</b>	16,337 (81.2)	1.8	3,775 (18.5)	3.6
<b>Low risk</b>	6 (3.2)	0	182 (96.8)	7.8
<b>Moderate risk</b>	1 (0)	0	50 (98)	21.7
<b>High risk</b>	0 (0)	0	14 (100)	24

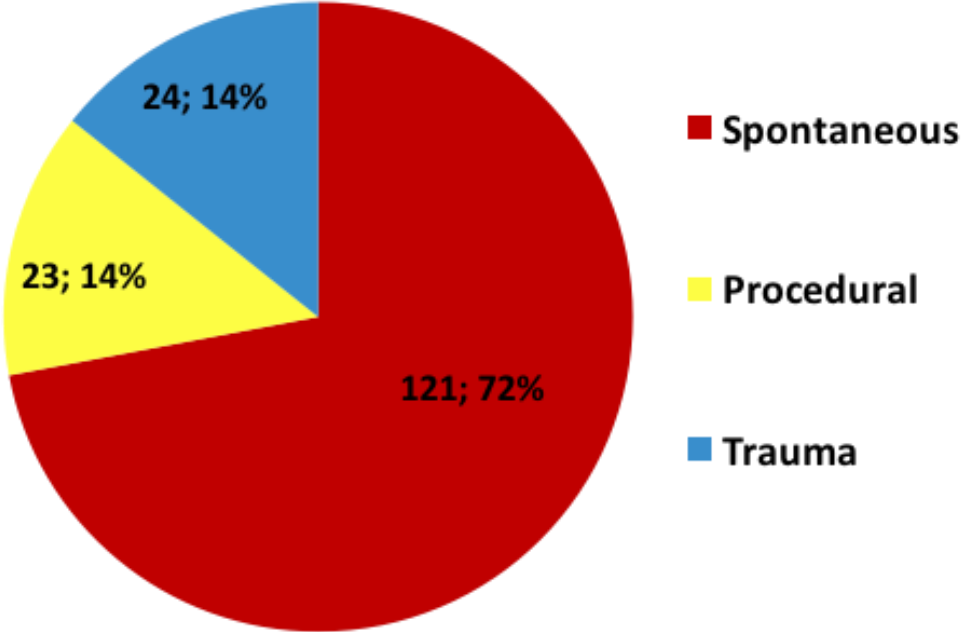
\* Based on anemia and history of spontaneous bleeding only

\*\* Absolute risk increase of TIMI major or minor bleeding, ticagrelor pooled vs. placebo

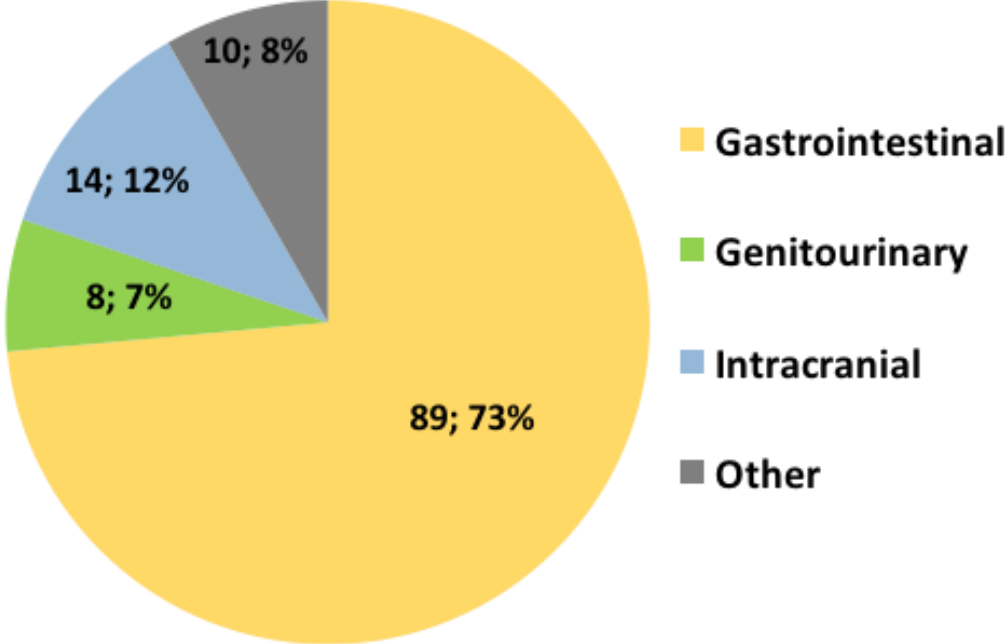
N = number, ARI = absolute risk increase, KM = Kaplan Maier

Figure S1. Etiology and Sites of TIMI major or minor bleeding in the Ticagrelor 60 mg group (Safety cohort).

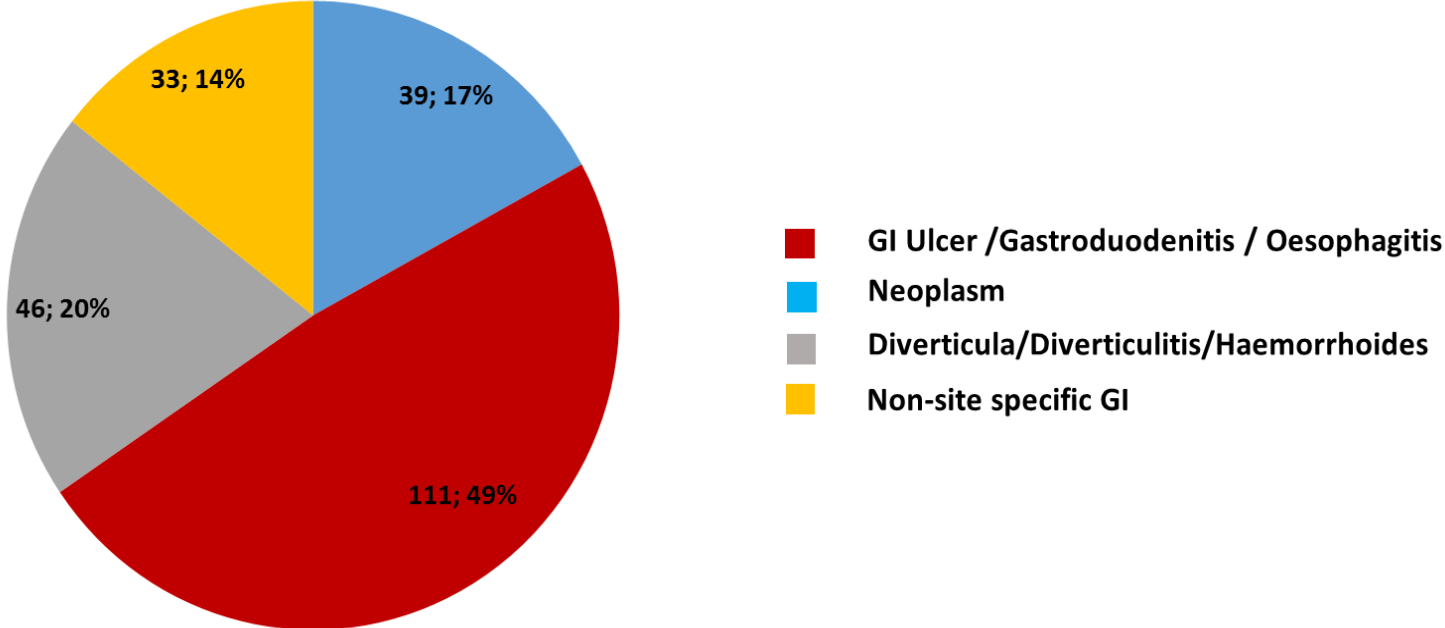
**A. Etiology**



**B. Site**



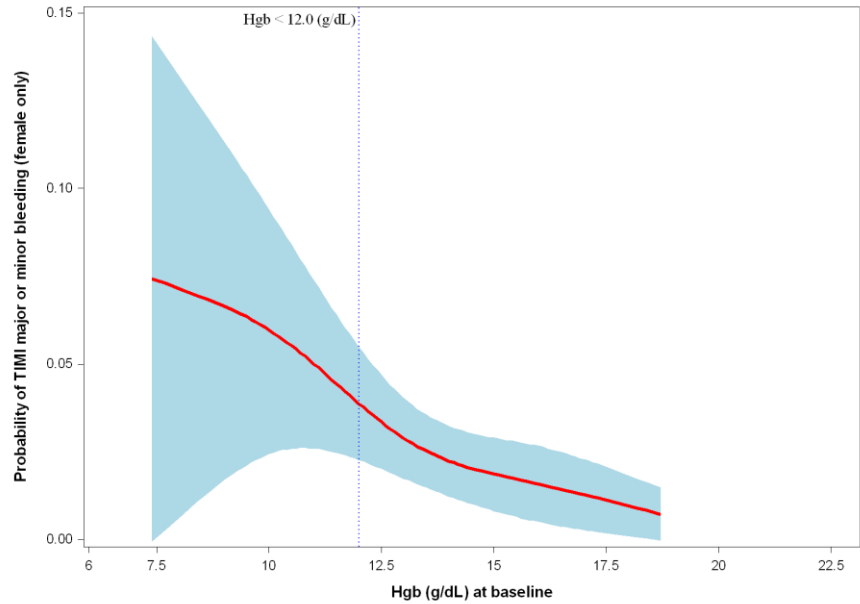
**Figure S2. Sites of spontaneous gastrointestinal TIMI major or minor Bleeding (doses pooled).**



GI= Gastrointestinal.

**Figure S3. Spline of hemoglobin and TIMI major or minor bleeding in women (a) and men (b), dashed lines at the cutpoint defined for anemia.**

A.



B.

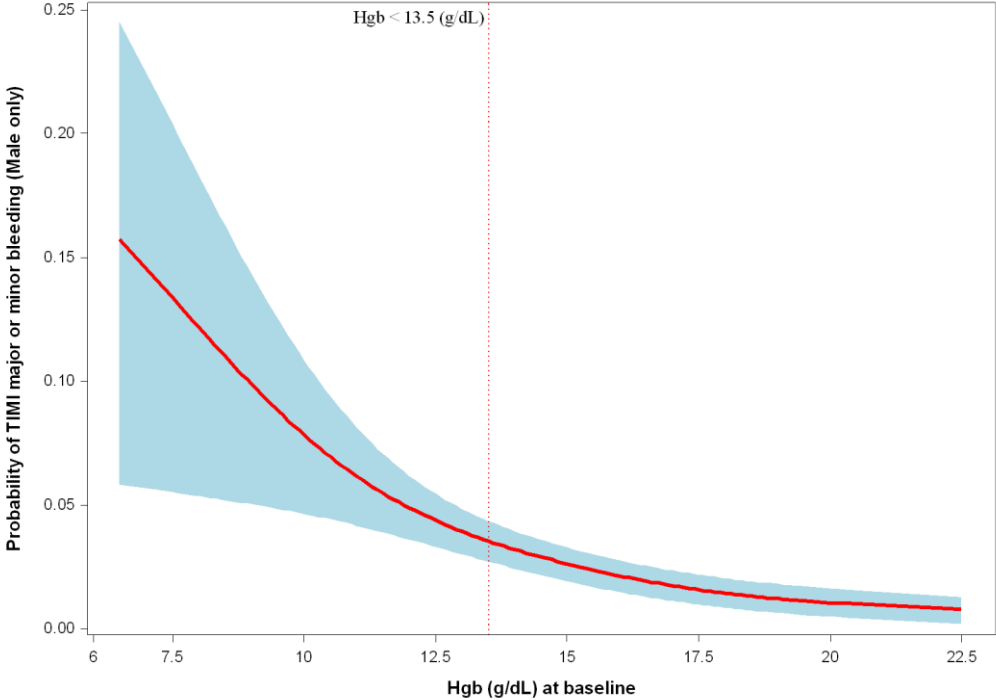




Figure S4. Instantaneous hazard for TIMI major or minor bleeding. HR=Hazard Ratio, TIMI=Thrombolysis in Myocardial Infarction.

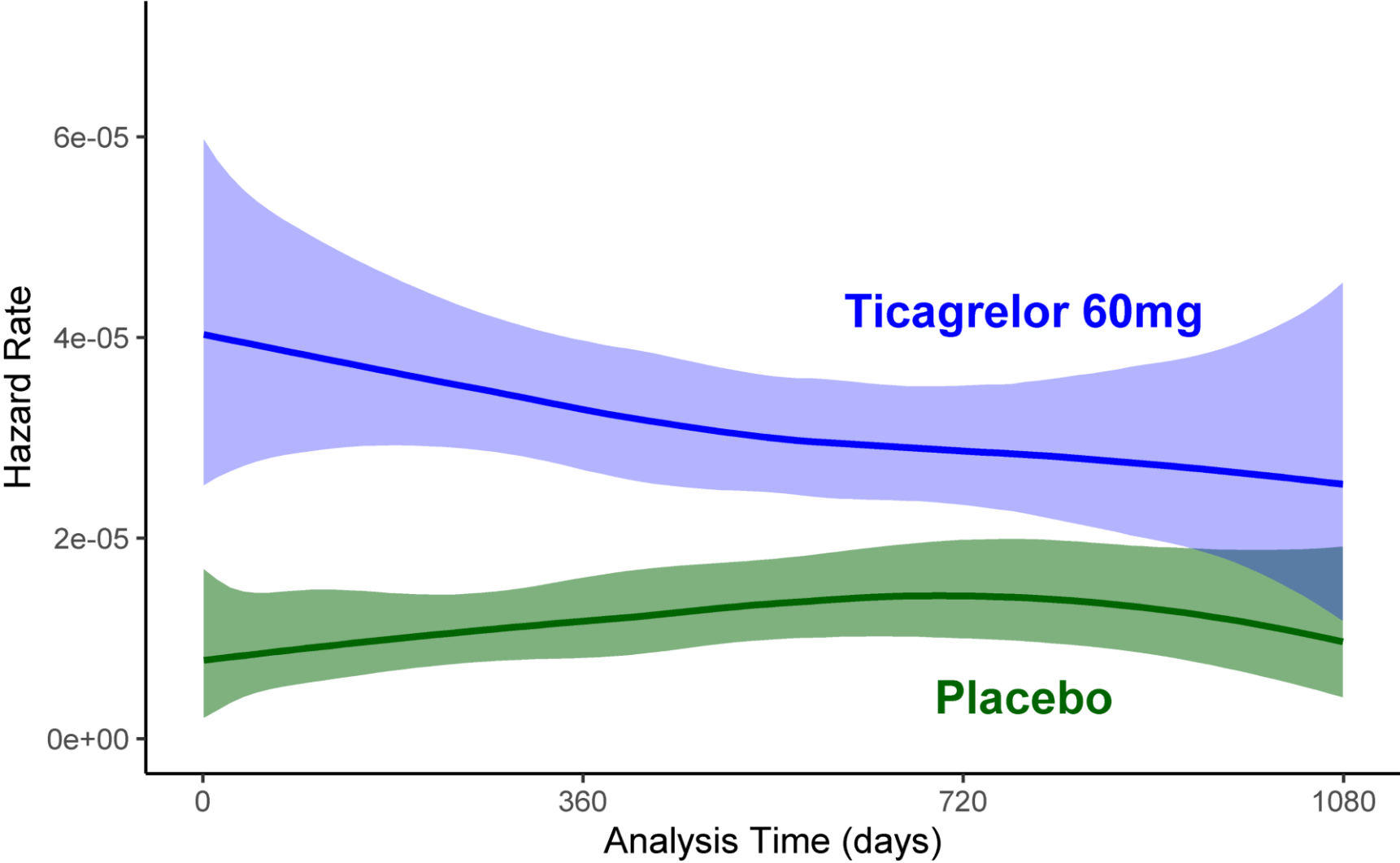
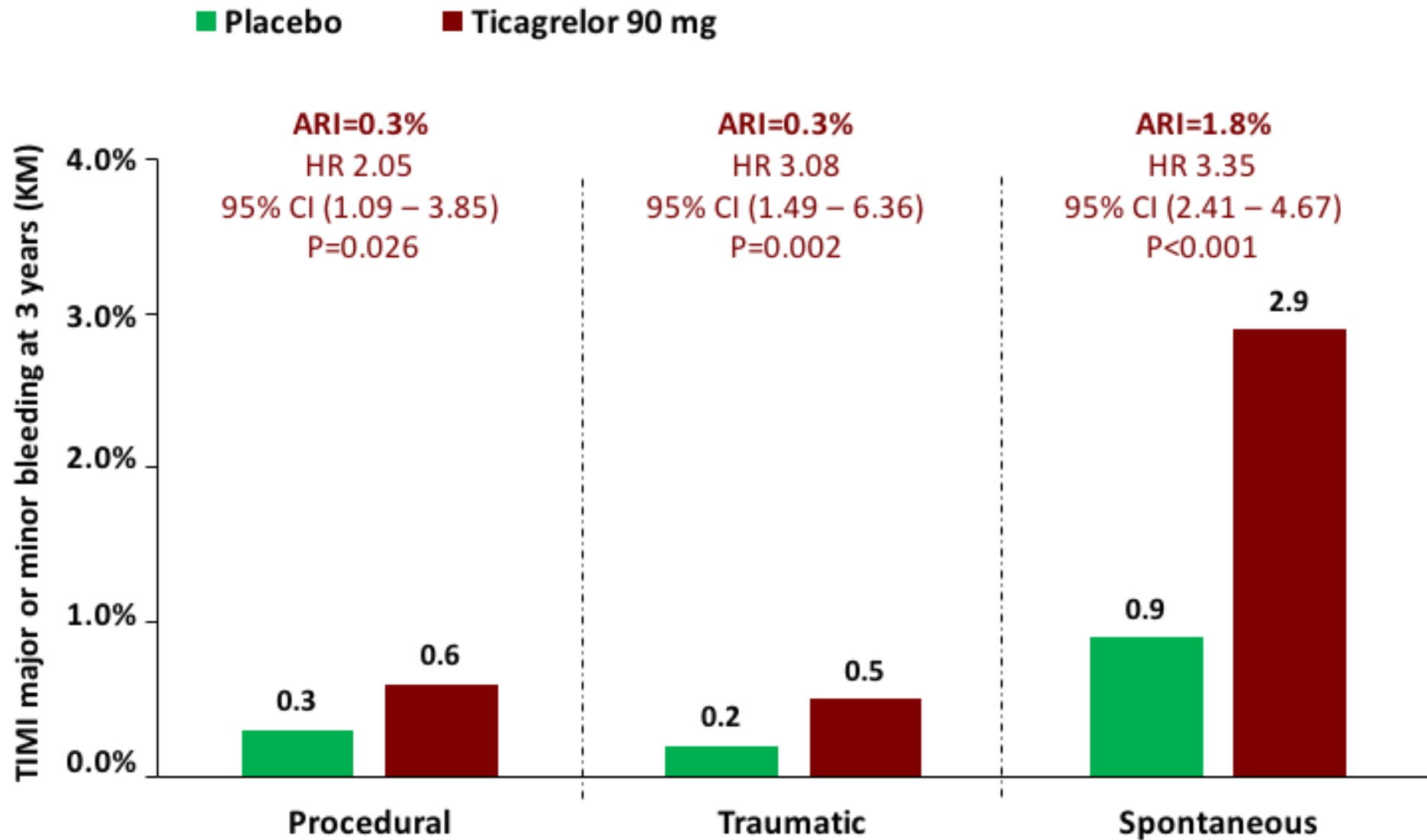


Figure S5. Sites (a) and etiologies (b) of TIMI major or minor bleeding, Ticagrelor 90 mg vs. placebo. HR=Hazard Ratio, CI=Confidence Interval, TIMI=Thrombolysis in Myocardial Infarction, ARI=Absolute risk Increase, KM=Kaplan Maier.



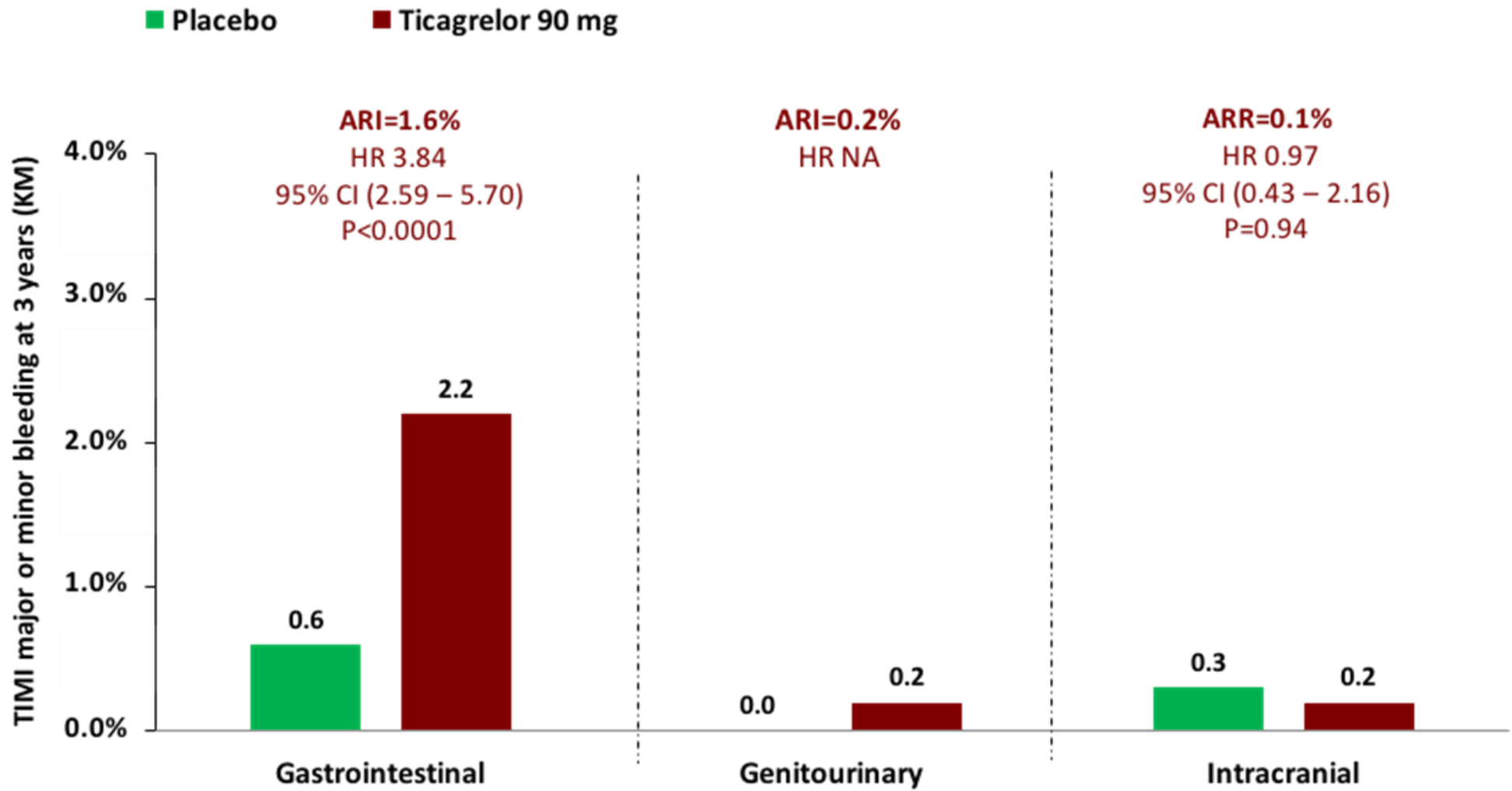


Figure S6. Bleeding and death, Ticagrelor 90 mg vs. placebo. HR=Hazard Ratio, CI=Confidence Interval, TIMI=Thrombolysis in Myocardial Infarction, KM=Kaplan Maier.

