Impact of an integrated treatment algorithm based on platelet function testing and clinical risk assessment: Results of the TRIAGE study

On behalf of the TRIAGE study Investigators

TRIAGE Patients Undergoing Percutaneous Coronary Interventions To Improve Clinical Outcomes Through Optimal Platelet Inhibition

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Disclosures

- *The presenting author has no financial conflicts to disclose*

STUDY ORGANIZATION

Multicenter prospective observational study

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BACKGROUND

- High on treatment platelet reactivity (HTPR) is associated with greater incidence of adverse cardiac events

- Platelet function testing alone for thienopyridine selection after PCI has not been shown to correlate with improved outcomes in randomized trials

- The role of platelet function testing *in the context of clinical risks* has not been investigated

STUDY OBJECTIVE

Compare outcomes in patients treated with *prasugrel vs. clopidogrel* at PCI following determination of platelet reactivity in conjunction with clinical risks:

- *Primary Efficacy Endpoint at 1 year*
  - **MACE** = composite of death, non-fatal MI, definite or probable stent thrombosis
- *Primary Safety Endpoint at 1 year*
  - **Bleeding** = BARC 2, 3 or 5

STUDY DESIGN

- Multicenter prospective observational study conducted over 3 sites from March 2012 to December 2014

- Main inclusion criterion: Chronic clopidogrel therapy for at least 2 weeks prior to elective or urgent PCI
- Main exclusion criterion: Cardiogenic shock

- Sample Size Assumption – 1 year MACE rate ~ 14% and a relative risk reduction with prasugrel ~ 40%, requiring 1000 patients. However due to slow enrollment, recruitment was terminated at 318 patients

METHODS

- PRU tested in the cath lab immediately prior to PCI with the VerifyNow assay.
- HTPR = PRU ≥ 230.
- Based on the study algorithm, treatment was continued with Clopidogrel or switched to Prasugrel (LD of 30 or 60mg).
- Follow up was by telephone at 1,6,12 months.
- Events were independently adjudicated.

STUDY ALGORITHM

- High ischemic risk was defined as any of the following criteria

a. PCI for ACS or stent thrombosis

b. High angiographic risk PCI (LM/Bifurcation PCI, ≥ 4 stents, thrombotic lesions)

c. 30 day stent thrombosis score of ≥6*

- High bleeding risk was defined as any of the following criteria

a. Bleeding risk score ≥ 10#

b. Recent surgery

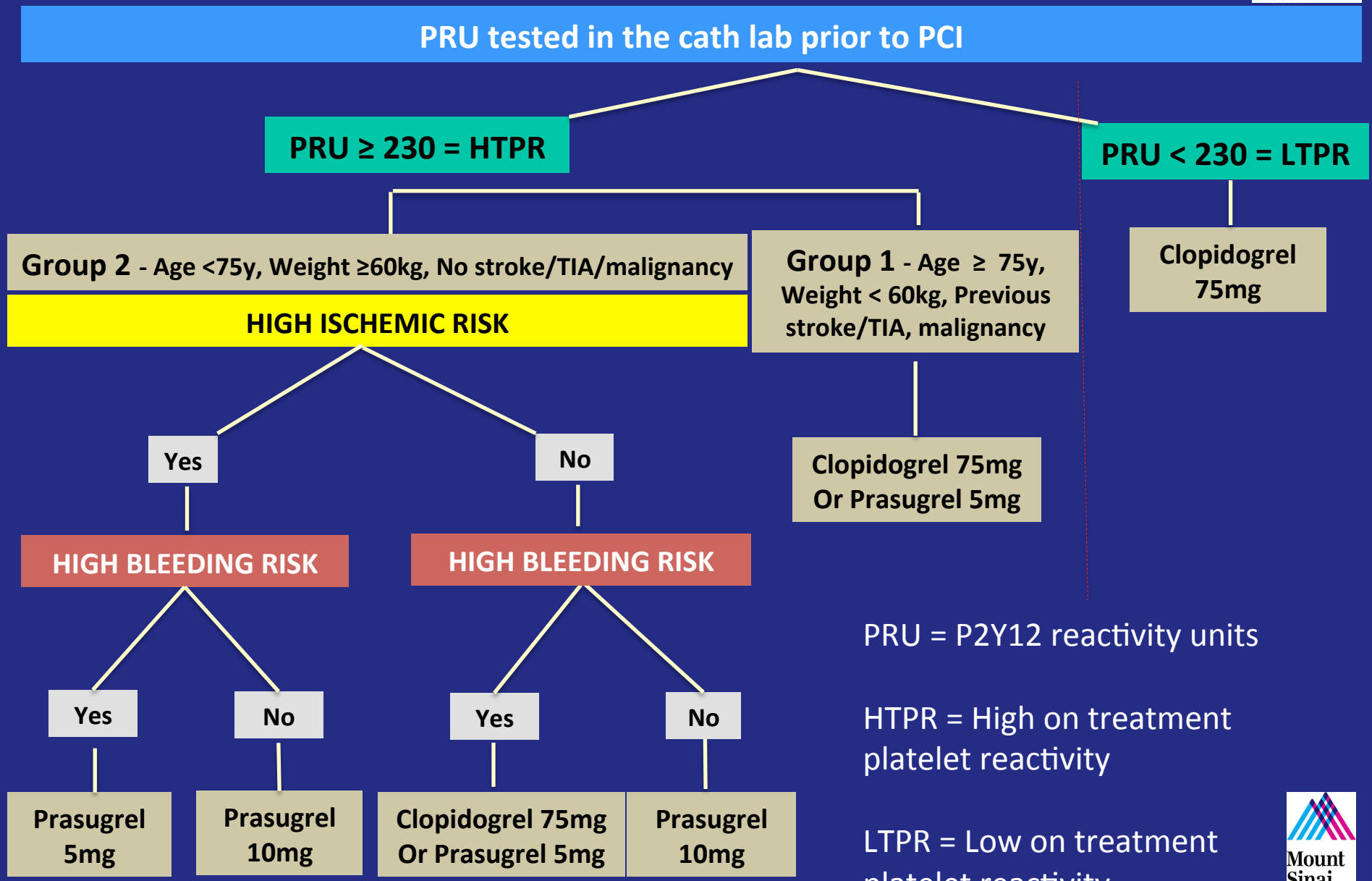
c. Recent bleeding history

d. Bleeding diathesis

*JACC Cardiovasc Interv. 2012 Nov;5(11):1097-105.

J Am Coll Cardiol. 2010 Jun 8;55(23):2556-66.

STUDY ALGORITHM



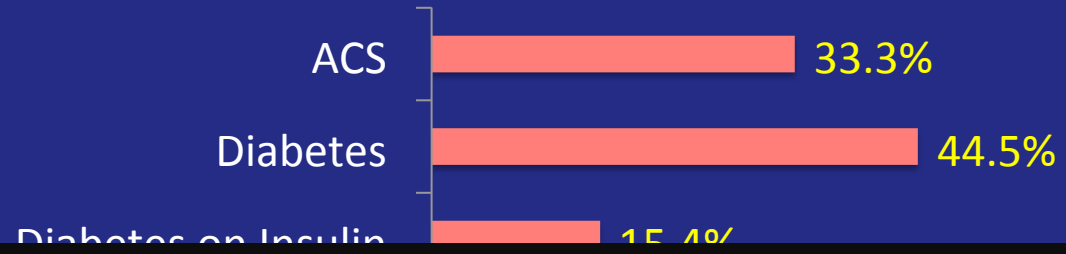
PRU = P2Y12 reactivity units

HTPR = High on treatment platelet reactivity

LTPR = Low on treatment platelet reactivity

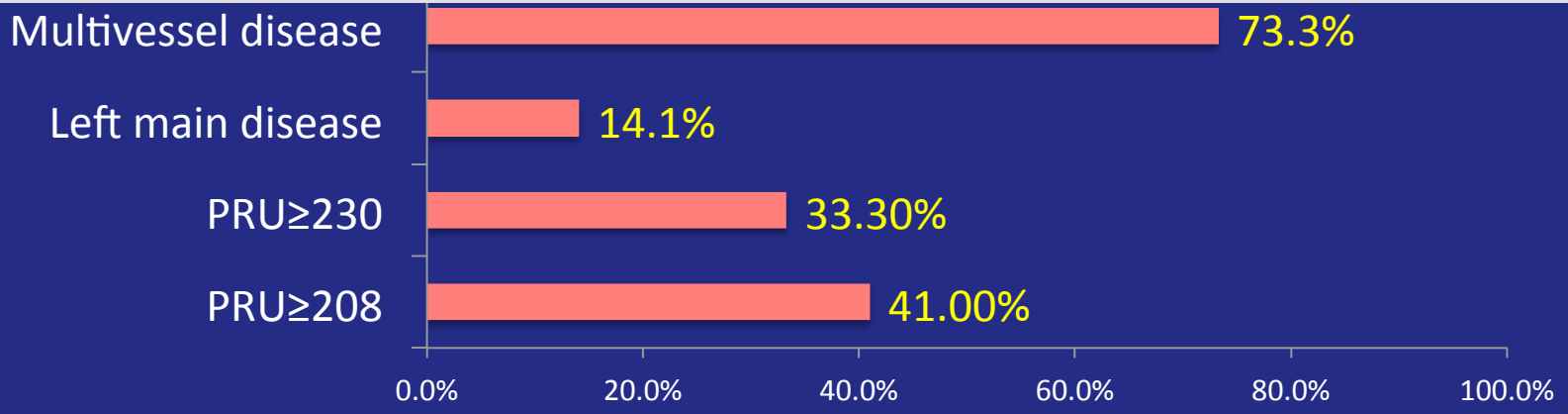
OVERALL COHORT

Mean age of 65.9 (9.8) years and 19.0% women.



40% patients at high ischemic risk by study criteria,
58% patients with PRU ≥230 and/or high ischemic risk by study criteria;
34% patients at high bleeding risk by study criteria

72% received Clopidogrel, 28% received Prasugrel



BASELINE CHARACTERISTICS

	Clopidogrel N = 228	Prasugrel N = 90	p
Age, mean (SD)	66.5 ±9.9	64.4 ± 9.3	0.06
Female gender, n (%)	40 (17.5)	20 (22.2)	0.21
Hypertension	208 (91.2)	84 (93.3)	0.62
Diabetes Mellitus	91 (39.9)	47 (52.2)	0.12
Dyslipidemia	198(86.8)	84 (93.3)	0.14
Prior MI	69 (30.3)	38 (42.2)	0.06
Prior PCI, n (%)	199 (87.3)	81 (90.0)	0.5
Prior CABG, n (%)	43 (18.9)	24 (26.7)	0.12
CKD, n (%)	22 (9.6)	7 (7.8)	0.77
Current smoker, n (%)	39 (17.1)	8 (8.9)	0.04
Heart failure, n (%)	14 (6.1)	12 (13.3)	0.04
BMI, mean (SD)	28.2 ±4.6	30.2 ±6.3	0.002
Prior stroke, n (%)	19 (8.3)	0 (0.0)	0.005
Baseline PRU, mean (SD)	148.9 ±76	290.1 ±48	<0.0001

PROCEDURAL CHARACTERISTICS

	Clopidogrel N = 228	Prasugrel N = 90	p
Multivessel disease, n (%)	166 (72.8)	67 (74.5)	0.87
Left main disease, n (%)	32 (14.4)	13 (14.0)	0.92
Stent thrombosis, n (%)	1 (0.4)	4 (4.4)	0.01
Femoral access, n (%)	219 (96.1)	87 (96.7)	0.77
Vascular closure device, n (%)	210 (92.1)	87 (96.7)	0.28
No. of vessels treated, mean (SD)	1.2 ± 0.5	1.3 ± 0.4	0.26
No. of lesions treated, mean (SD)	1.7 ± 0.9	1.6 ± 0.8	0.73
No. of stents implanted, mean (SD)	1.7 ± 0.98	1.6 ± 0.8	0.14
Total stent length, mm, mean (SD)	34.8 ± 23.6	31.9 ± 23.7	0.33
Stent type used: DES only, n (%)	217 (95.2)	83 (92.2)	0.28
Procedural anti-thrombotic therapy			
Heparin, n (%)	62 (27.2)	16 (17.8)	0.08
Bivalirudin, n (%)	109 (47.8)	67 (74.4)	<0.0001
Glycoprotein IIb/IIIa inhibitor, n (%)	8 (3.5)	2 (2.2)	0.55

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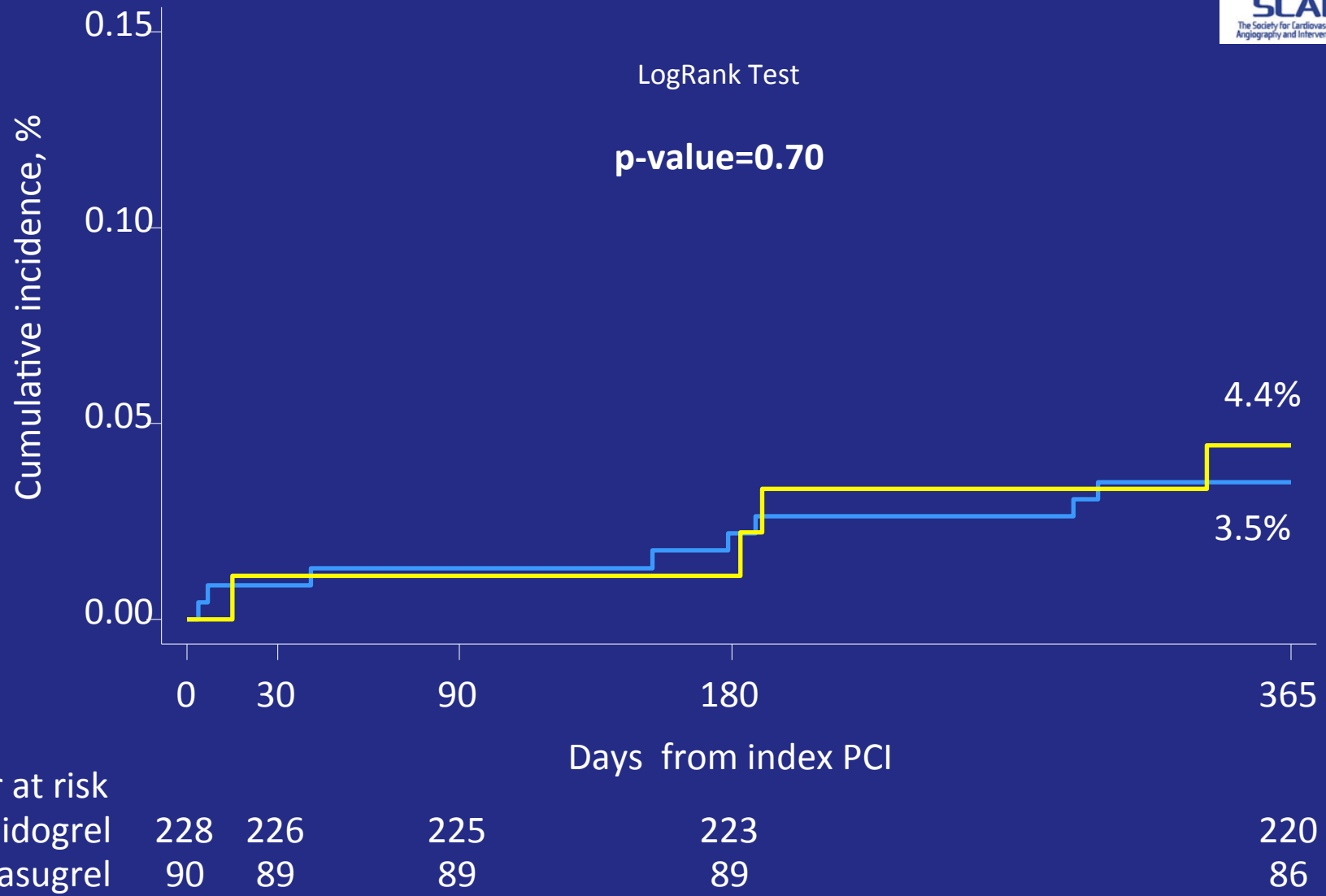
1 YEAR CLINICAL OUTCOMES

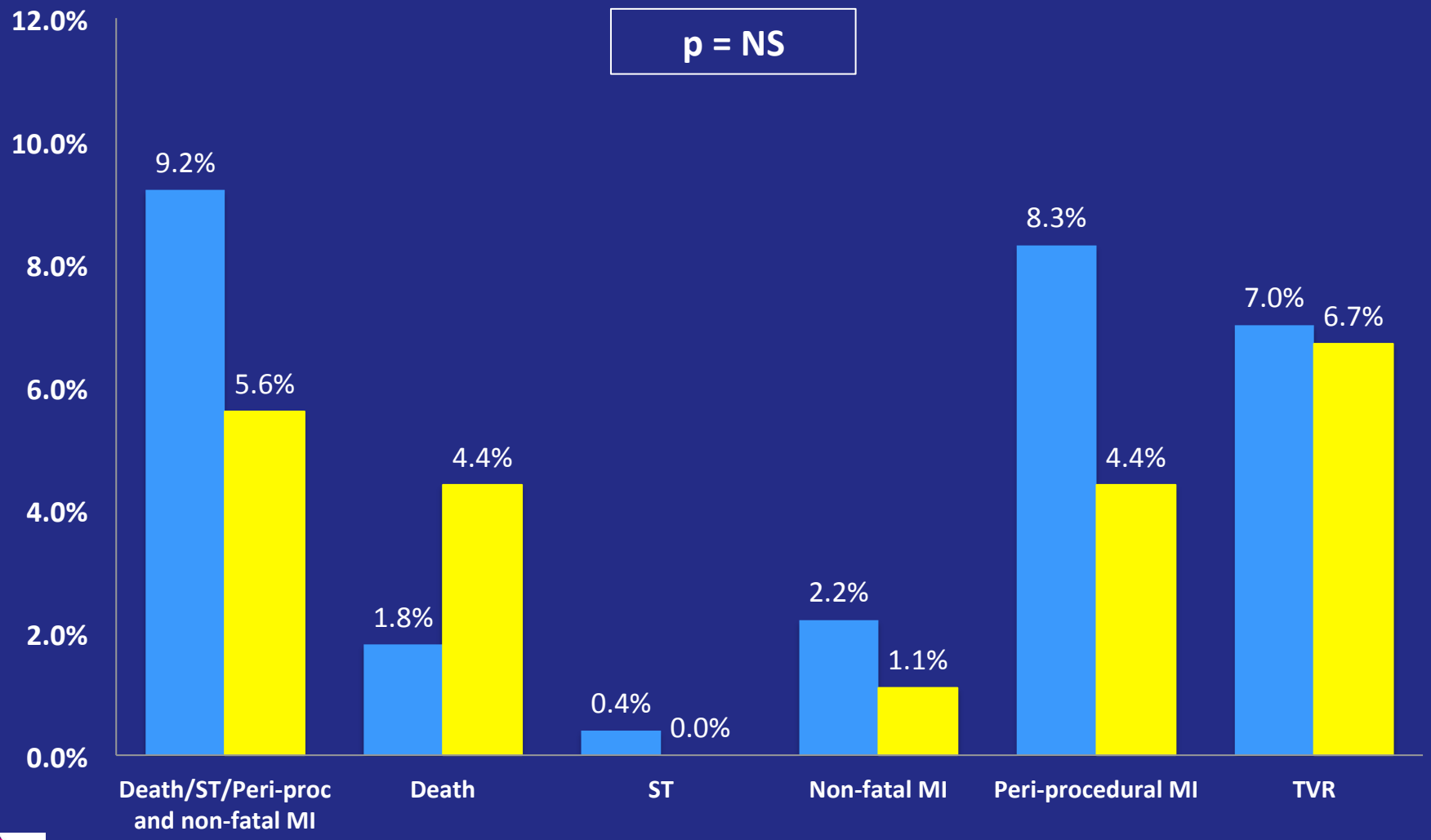
	Clopidogrel N = 228	Prasugrel N = 90	p
Ischemic outcomes*			
Death/Non-fatal MI/ST	8 (3.5)	4 (4.4)	0.70
Death	4 (1.8)	4 (4.4)	0.17
Non-fatal MI	5 (2.2)	1 (1.1)	0.52
Stent thrombosis	1 (0.4)	0 (0.0)	0.53
Clinically driven TVR	16 (7.0)	6 (6.7)	0.88
Death/Non-fatal MI/ST/TVR	22 (9.7)	10 (11.1)	0.73
Bleeding outcomes*			
BARC 2, 3 or 5	18 (7.9)	5 (5.6)	0.47
BARC 3 or 5	10 (4.4)	1 (1.1)	0.15
Any BARC bleed	32 (14.0)	8 (8.9)	0.21
TIMI Major	10 (4.4)	1 (1.1)	0.15
ACUITY Major	11 (4.8)	1 (1.1)	0.21

*Numbers are presented as **n (%)**

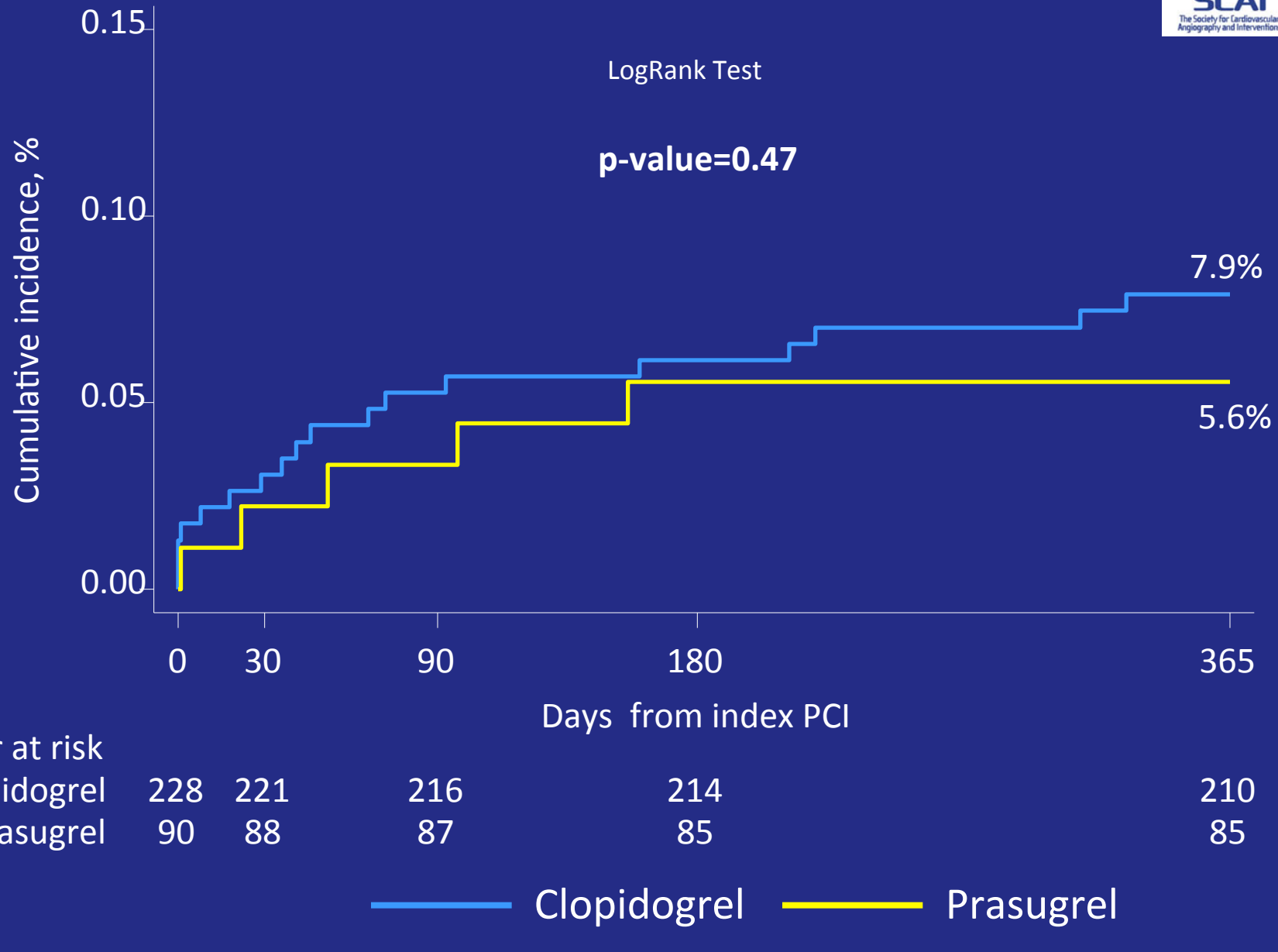
Primary efficacy endpoint: MACE (Death, Non-fatal MI, ST)



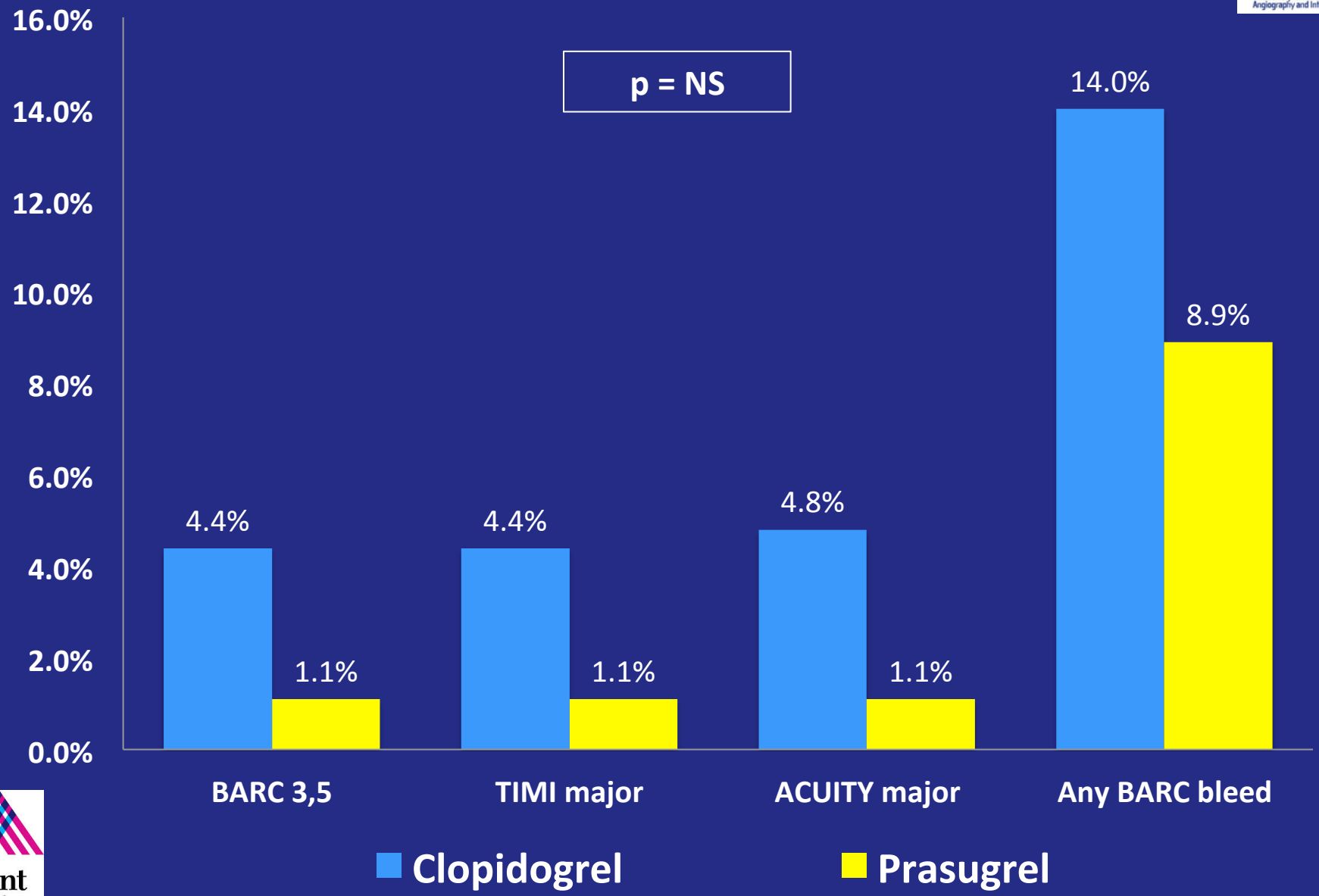
Secondary Ischemic Endpoints



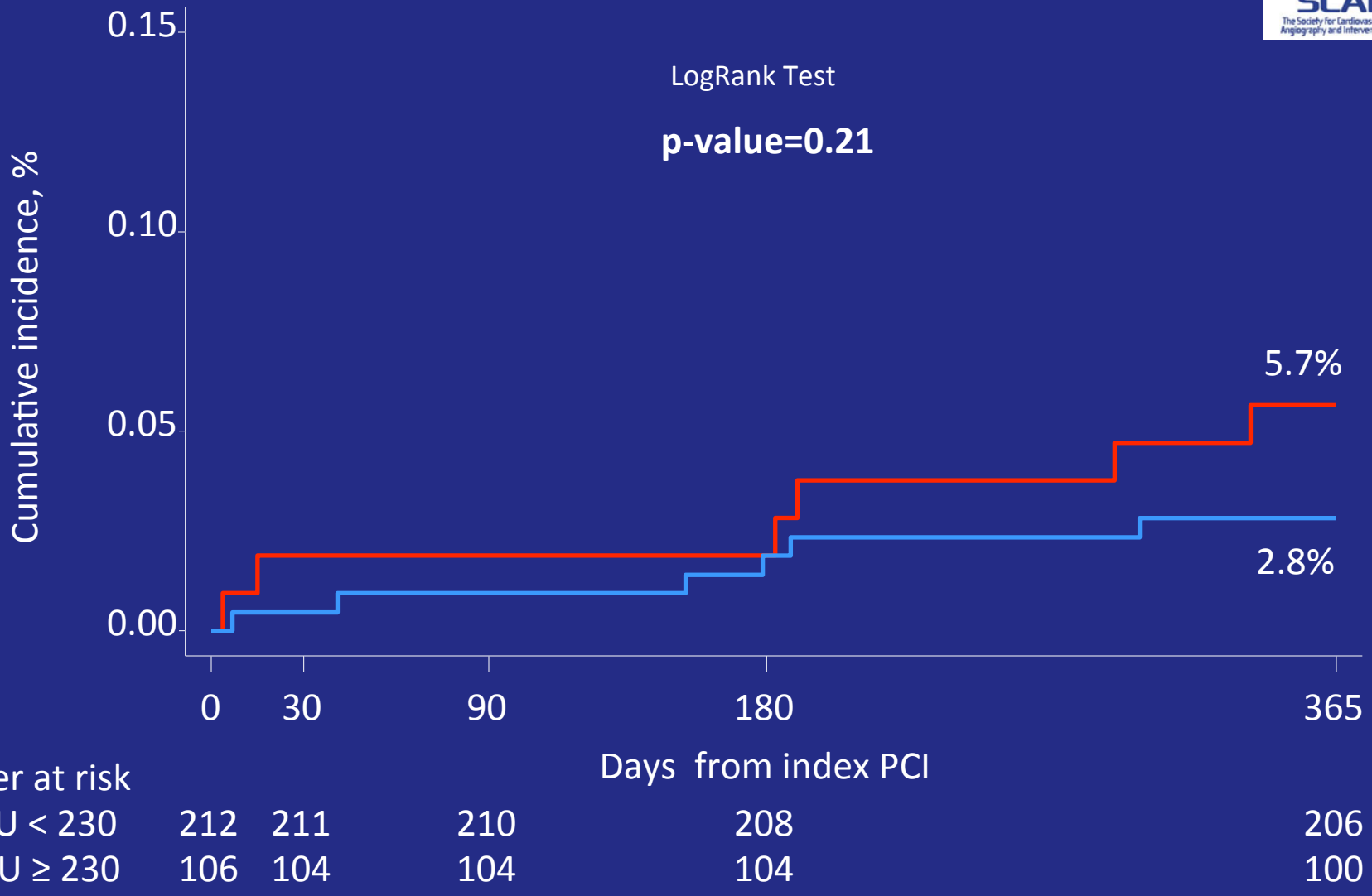
Primary Safety Endpoint: BARC bleeding 2,3 or 5



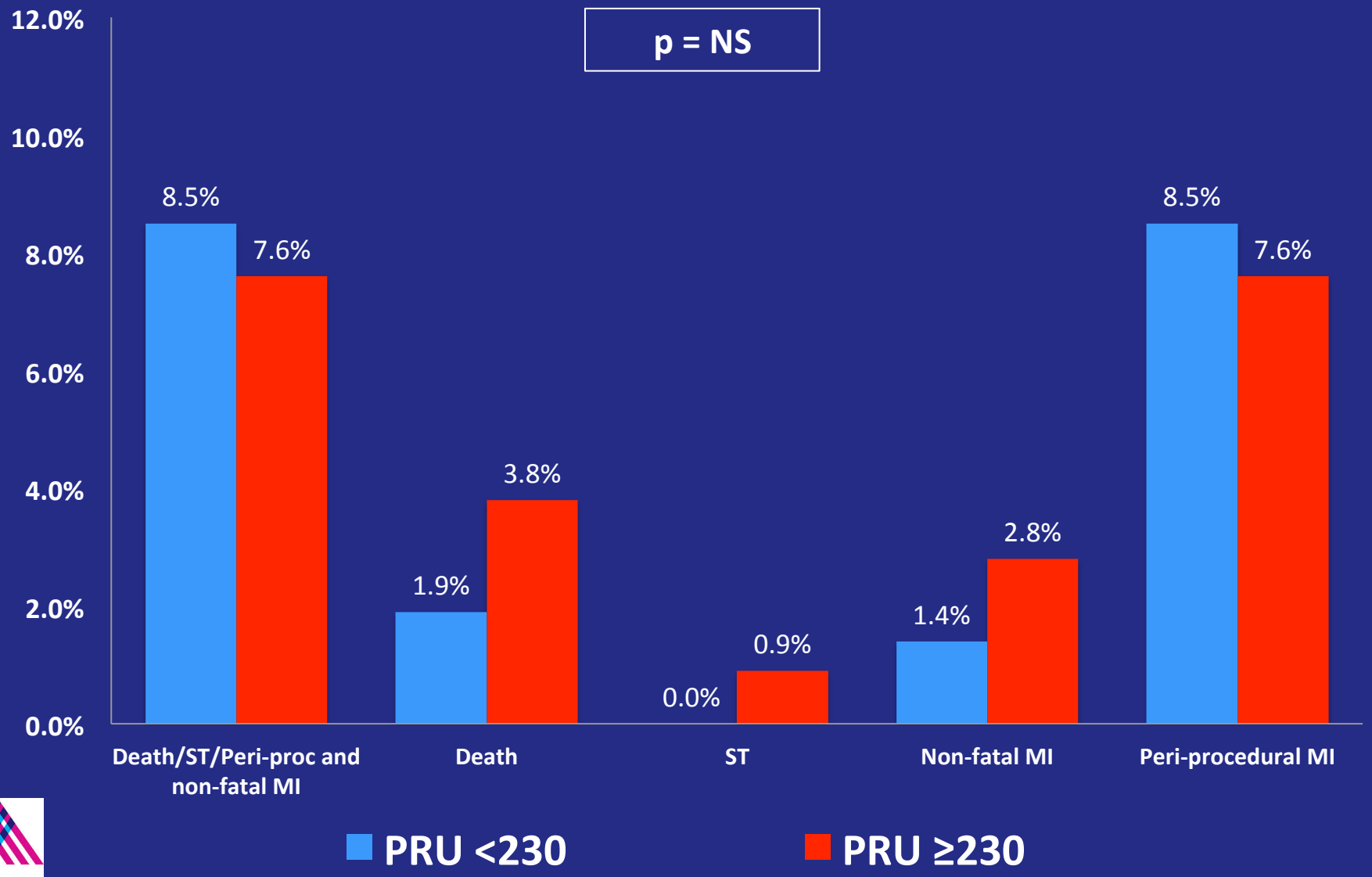
Secondary Bleeding Endpoints



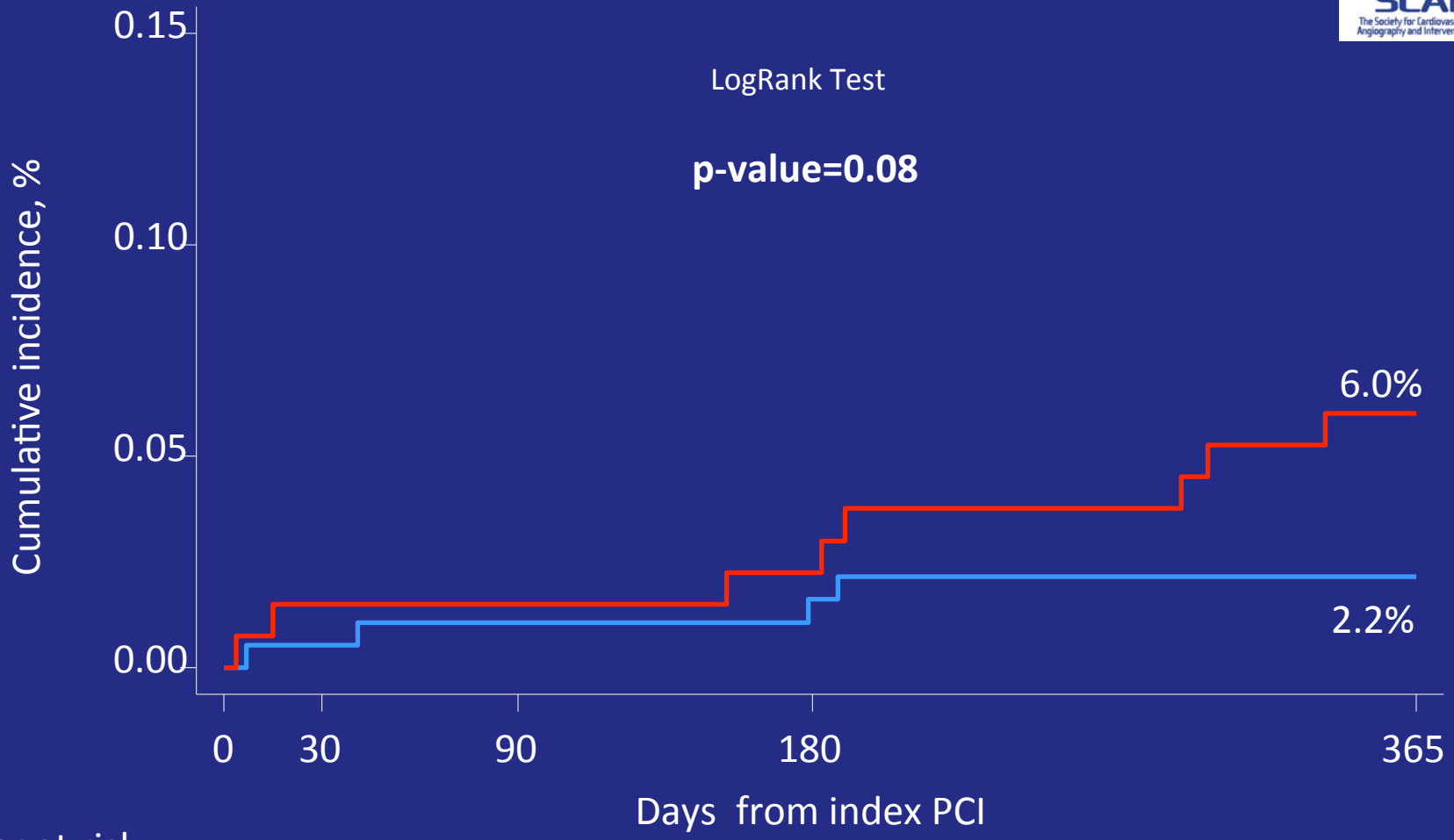
PRU Cut-off 230: MACE (Death, Non-fatal MI, ST)



PRU Cut-off 230: Secondary Ischemic Endpoints



PRU Cut-off 208: MACE (Death, Non-fatal MI, ST)

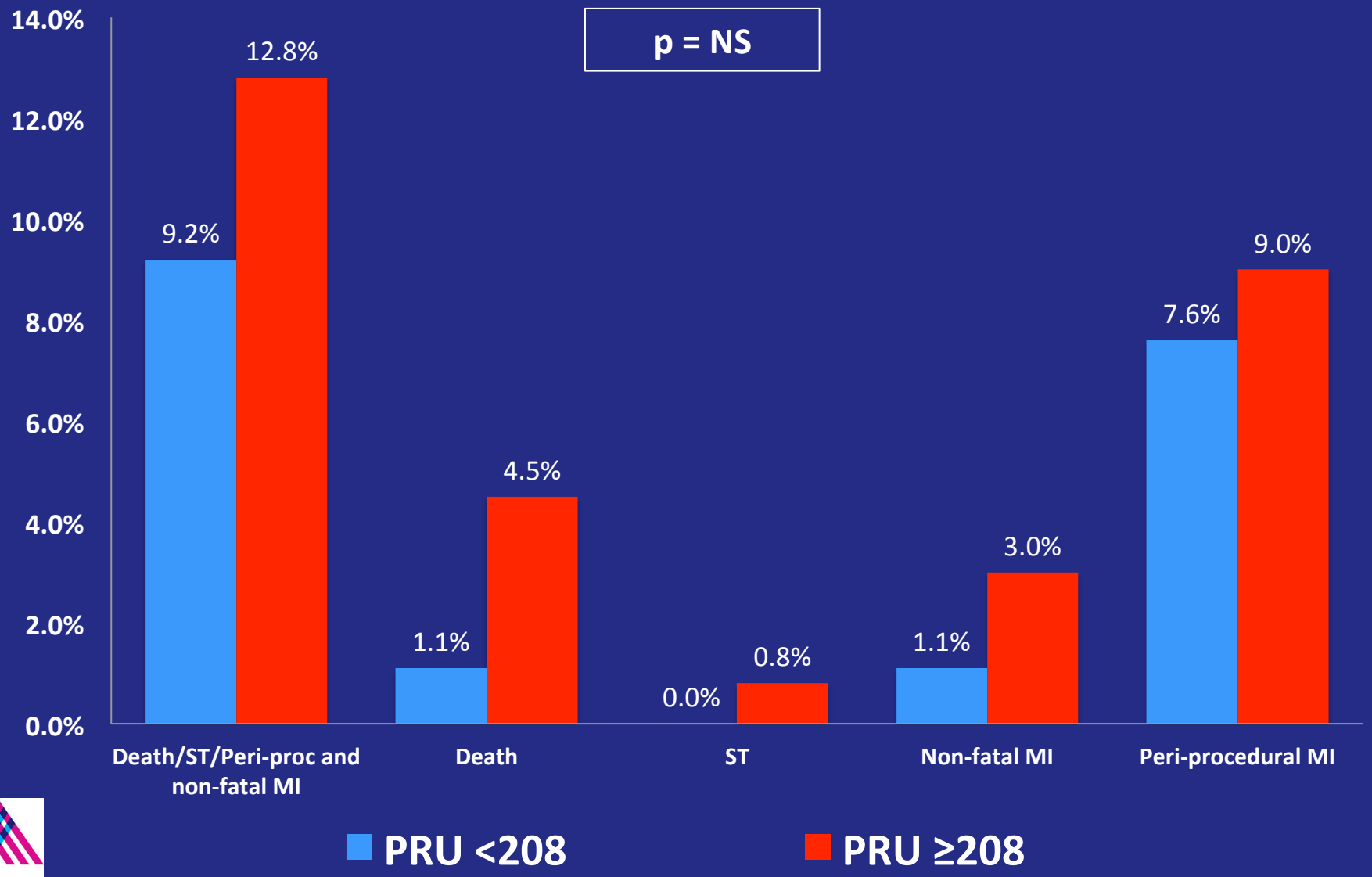


Number at risk

PRU<208	185	184	183	182	181
PRU ≥ 208	133	131	131	130	125

PRU < 208 PRU ≥ 208

PRU Cut-off 208: Secondary Ischemic Endpoints



CONCLUSIONS

- Use of a clinical risk algorithm to triage real-world PCI patients for choice and intensity of thienopyridine prescription resulted in similar ischemic outcomes in HTPR patients receiving prasugrel and primarily LTPR patients on clopidogrel.

- There was no untoward increase in bleeding with prasugrel compared with clopidogrel.

LIMITATIONS

- Low enrollment, underpowered study – precluding definitive conclusions.
- Observational design, unblinded prescription of therapy.
- Low event rate for the primary endpoint despite an all-comer high-risk population – predominant 2nd gen. DES use.
- Use of an unvalidated study treatment algorithm - albeit incorporating ischemic and bleeding risk scores validated in ACS.

IMPLICATIONS

- When Prasugrel is prescribed to carefully selected ACS and non-ACS PCI patients, there is no untoward increase in bleeding
- Use of platelet function testing may identify more patients at a high ischemic risk, than clinical assessment alone
- The best PRU cut-off for HTPR in a real world unselected population for risk-prognostication is undetermined
- The effect of a tailored integrated assessment for thienopyridine prescription needs randomized examination in future trials

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