



ACTION Study Group
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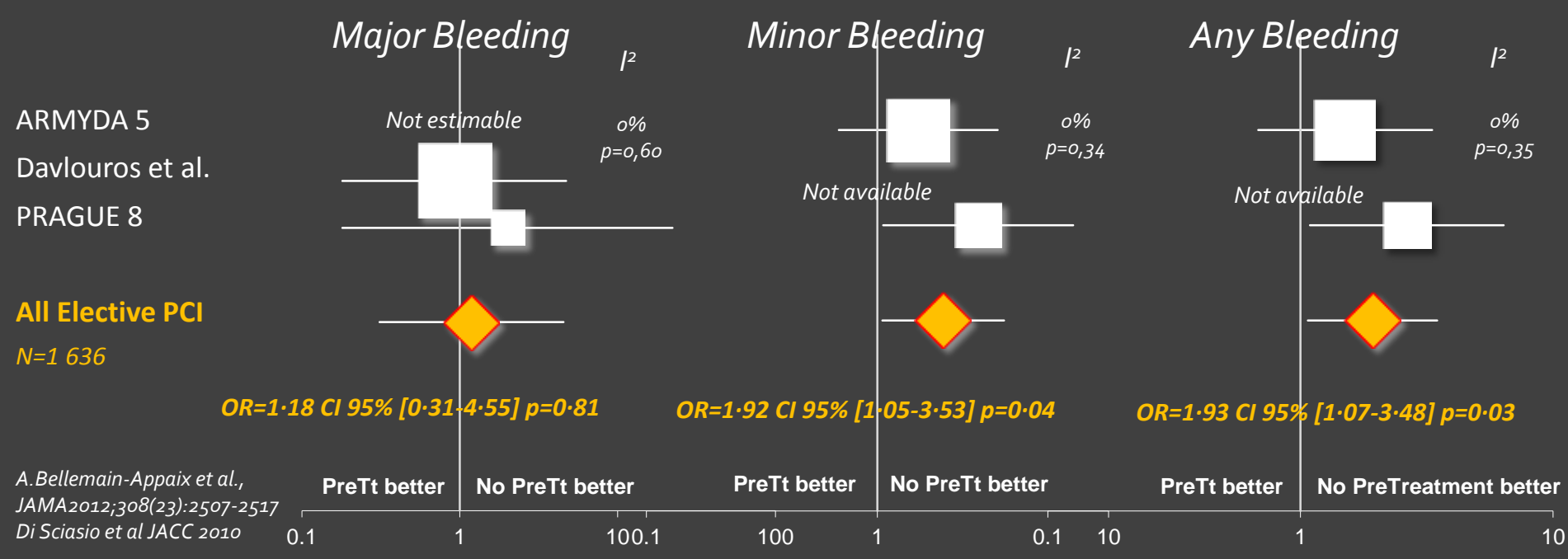
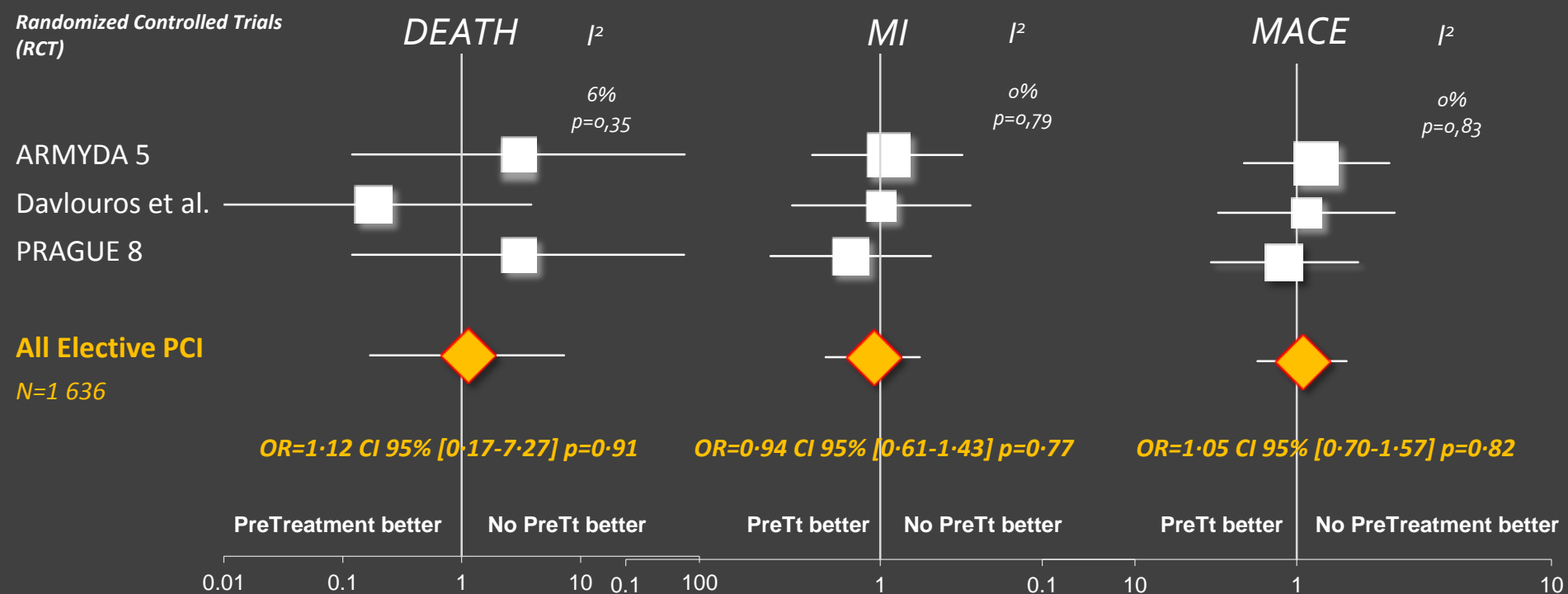


Preloading with prasugrel: no benefits,
potential harm!

P2Y12 Pre-treatment ESC Recommendations

Title	Citation		Class	LOE
2011 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation	European Heart Journal 2011;32:2999–3054	“A P2Y12 inhibitor as soon as possible”	I	A
		Clopidogrel 600mg	I	B
		Ticagrelor	I	B
2010 ESC/EACTS guidelines on myocardial revascularization	European Heart Journal 2010;31:20:2501–2555	“Clopidogrel 600mg as soon as possible”	I	C

Randomized Controlled Trials (RCT)



A. Bellemain-Appaix et al., JAMA 2012;308(23):2507-2517
Di Sciasio et al JACC 2010



The ACCOAST Trial



ACCOAST design

NSTEMI + Troponin ≥ 1.5 times ULN local lab value
Clopidogrel naive or on long term clopidogrel 75 mg

n~4100 (event driven)

Randomize 1:1
Double-blind

Prasugrel 30 mg

Placebo

**Coronary
Angiography**

**Coronary
Angiography**

CABG
or
Medical
Management
(no more prasugrel)

CABG
or
Medical
Management
(no prasugrel)

Prasugrel 30 mg

Prasugrel 60 mg

PCI

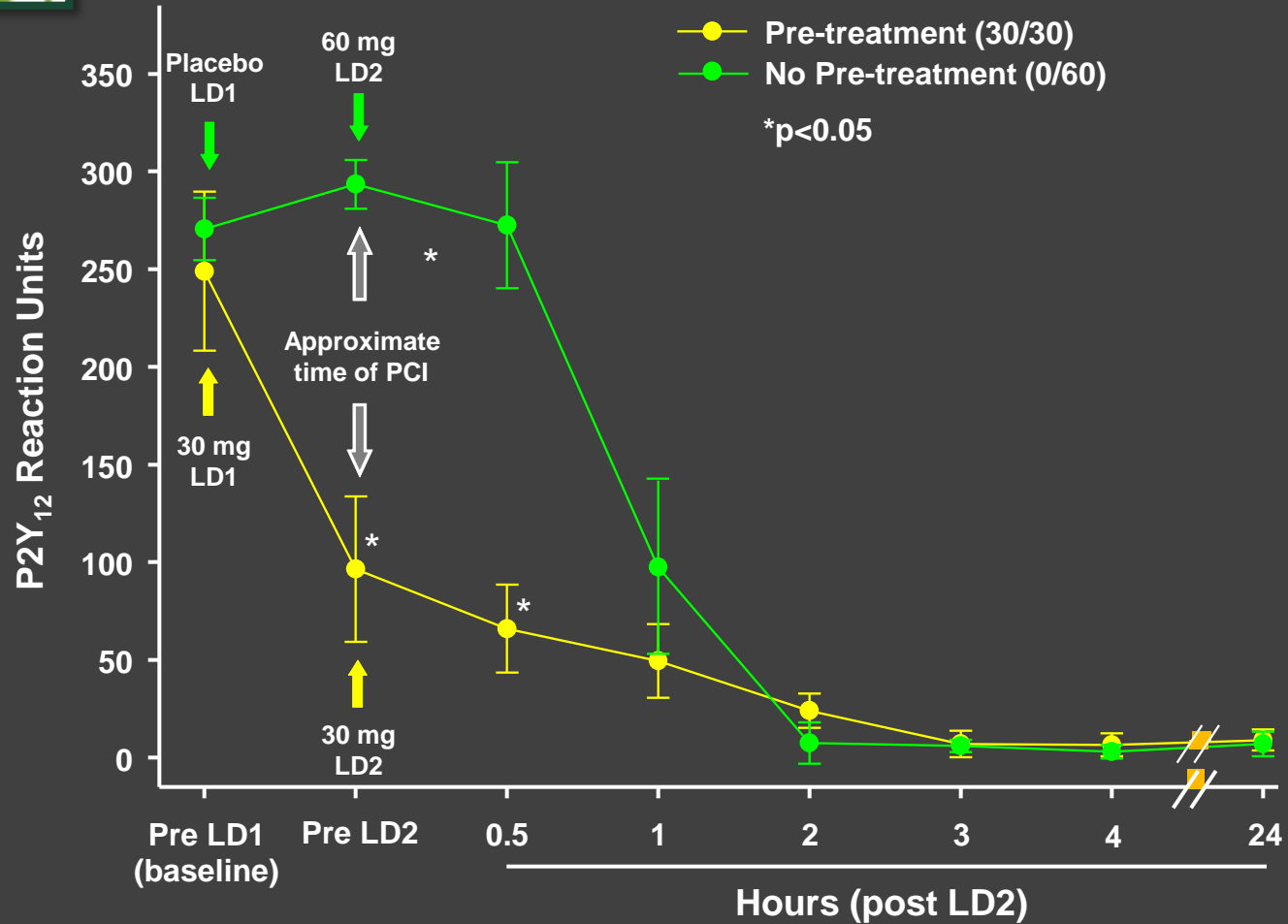
PCI

Prasugrel 10 mg or 5 mg (based on weight and age) for 30 days

1° Endpoint: CV Death, MI, Stroke, Urg Revasc, GP IIb/IIIa bailout, at 7 days



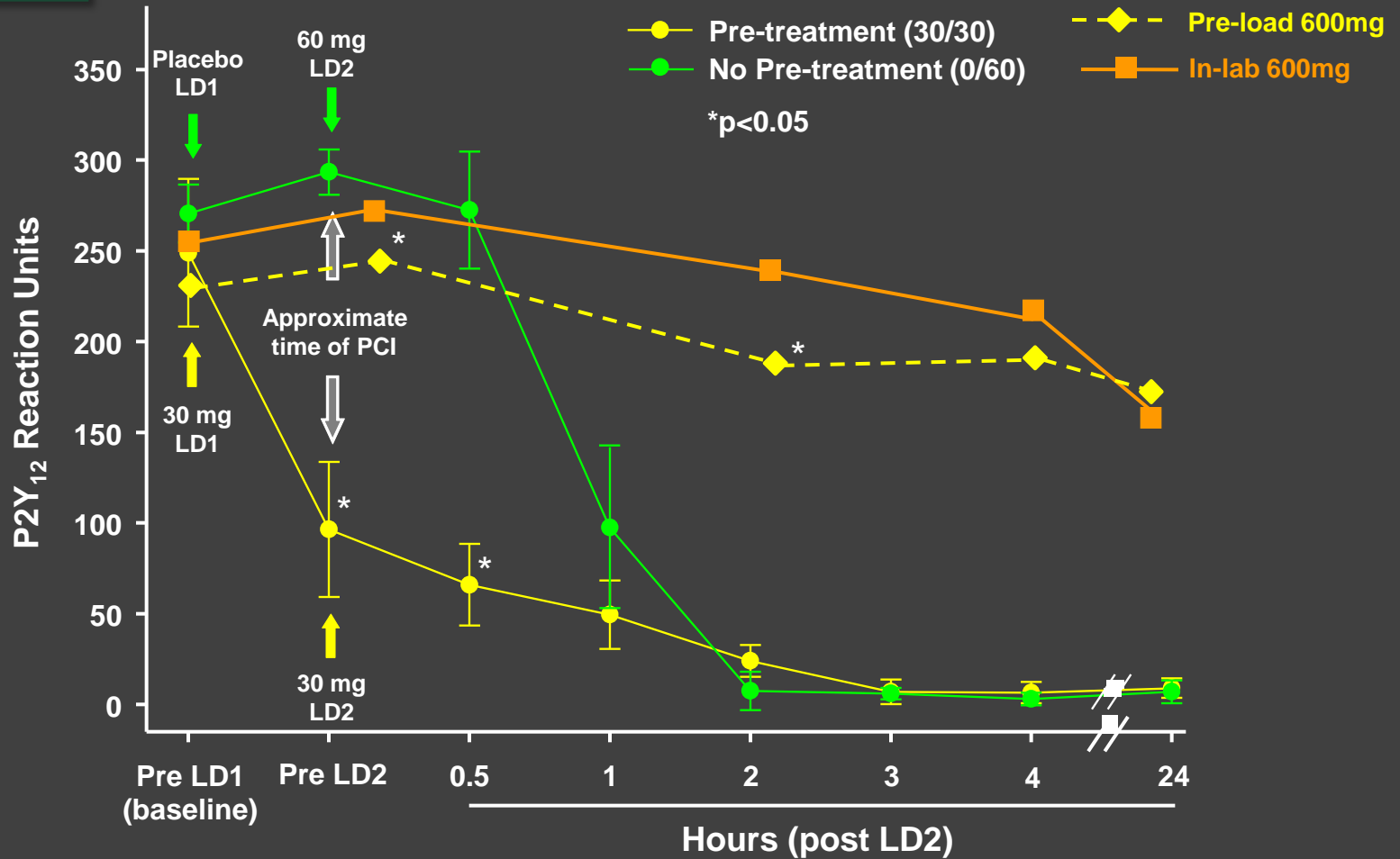
Pharmacodynamic sub-study



Data presented as median ± SEM. * p < 0.05 relative to the No pre-treatment group.
Pretreatment=Prasugrel 30 mg/Prasugrel 30 mg; No Pre-treatment=Placebo/Prasugrel 60 mg



Pharmacodynamic sub-study



Data presented as median \pm SEM. * p<0.05 relative to the No pre-treatment group.
 Pretreatment=Prasugrel 30 mg/Prasugrel 30 mg; No Pre-treatment=Placebo/Prasugrel 60 mg



Baseline Characteristics

Characteristics	Pre-treatment (N =2037)	No Pre-treatment (N =1996)
Age (mean, yrs)	64	64
Female sex (%)	27	28.0
Weight (mean, kg)	82	82
BMI \geq 30 (%)	29	28
CV risk factors (%)		
Diabetes mellitus	20	20
Dyslipidemia	45	45
Hypertension	63	61
Current smoker	34	33
Region of enrolment (%)		
Eastern Europe/Israel	42	42
Western Europe/Canada	58	58

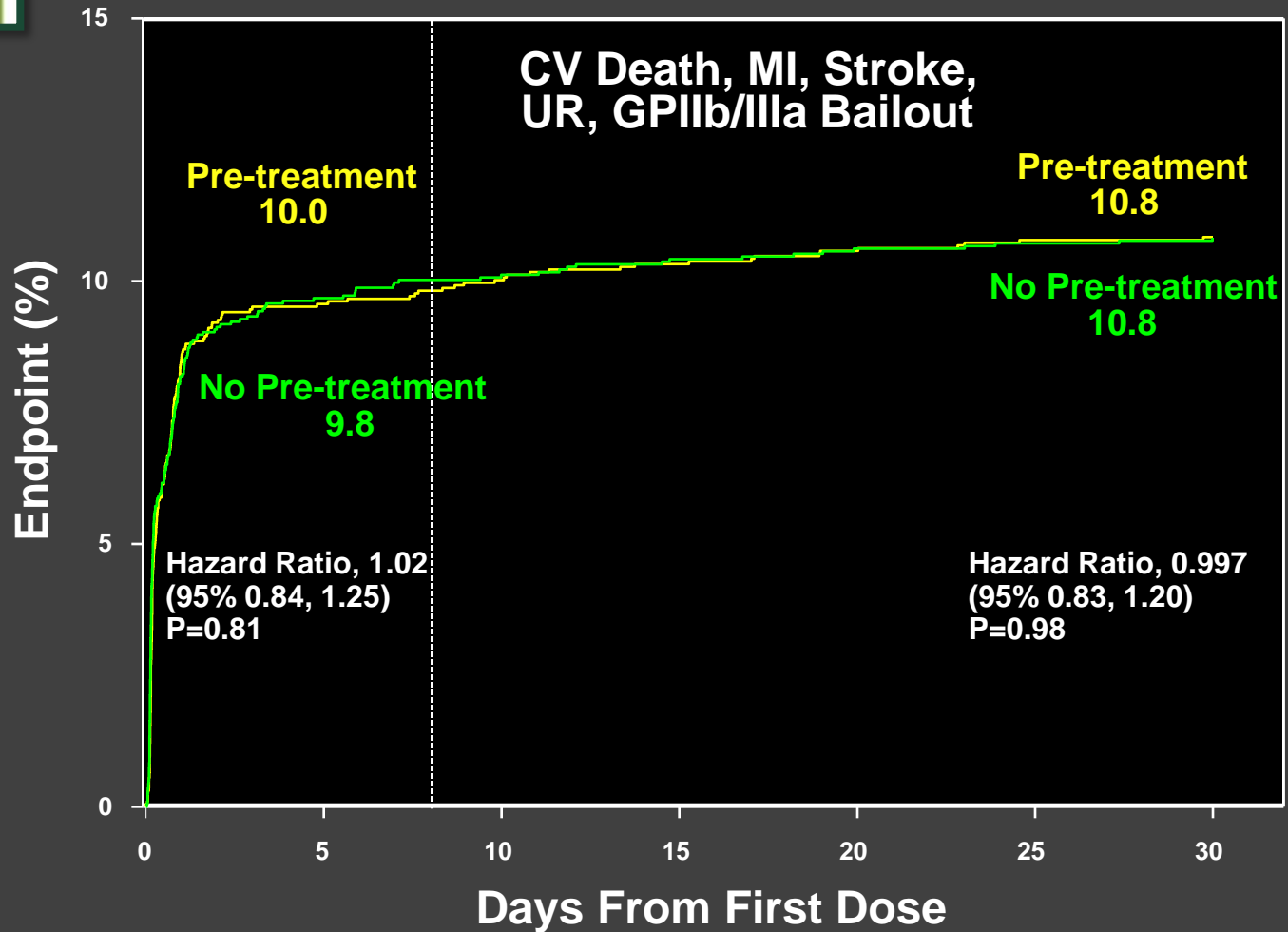


Baseline Characteristics

Characteristics	Pre-treatment (N =2037)	No Pre-treatment (N =1996)
GRACE score (%)		
<140	76	78
≥140	24	22
CRUSADE score (median)	34	34
Timing (hr)		
→Symptom onset to 1st LD, median	14.6	15.2
→ 1 st LD to coronary angiogram, median	4.4	4.2
Access (%)		
Femoral	57	57
Radial	43	43



1° Efficacy End Point @ 7 + 30 days (All Patients)

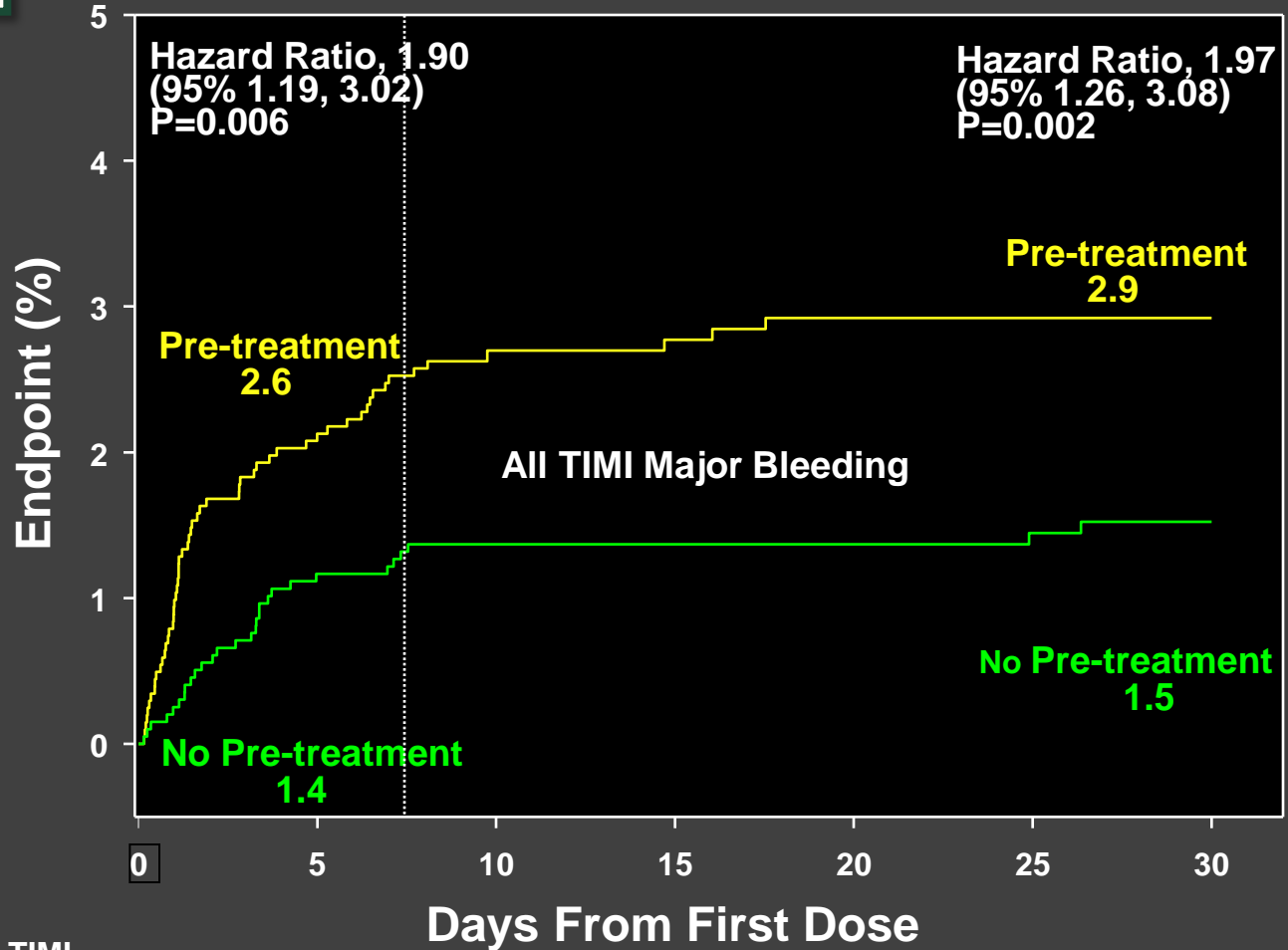


No. at Risk, Primary Efficacy End Point:

No pre-treatment	1996	1788	1775	1769	1762	1752	1621
Pre-treatment	2037	1821	1809	1802	1797	1791	1616



All TIMI (CABG or non-CABG) Major Bleeding (All Treated patients)



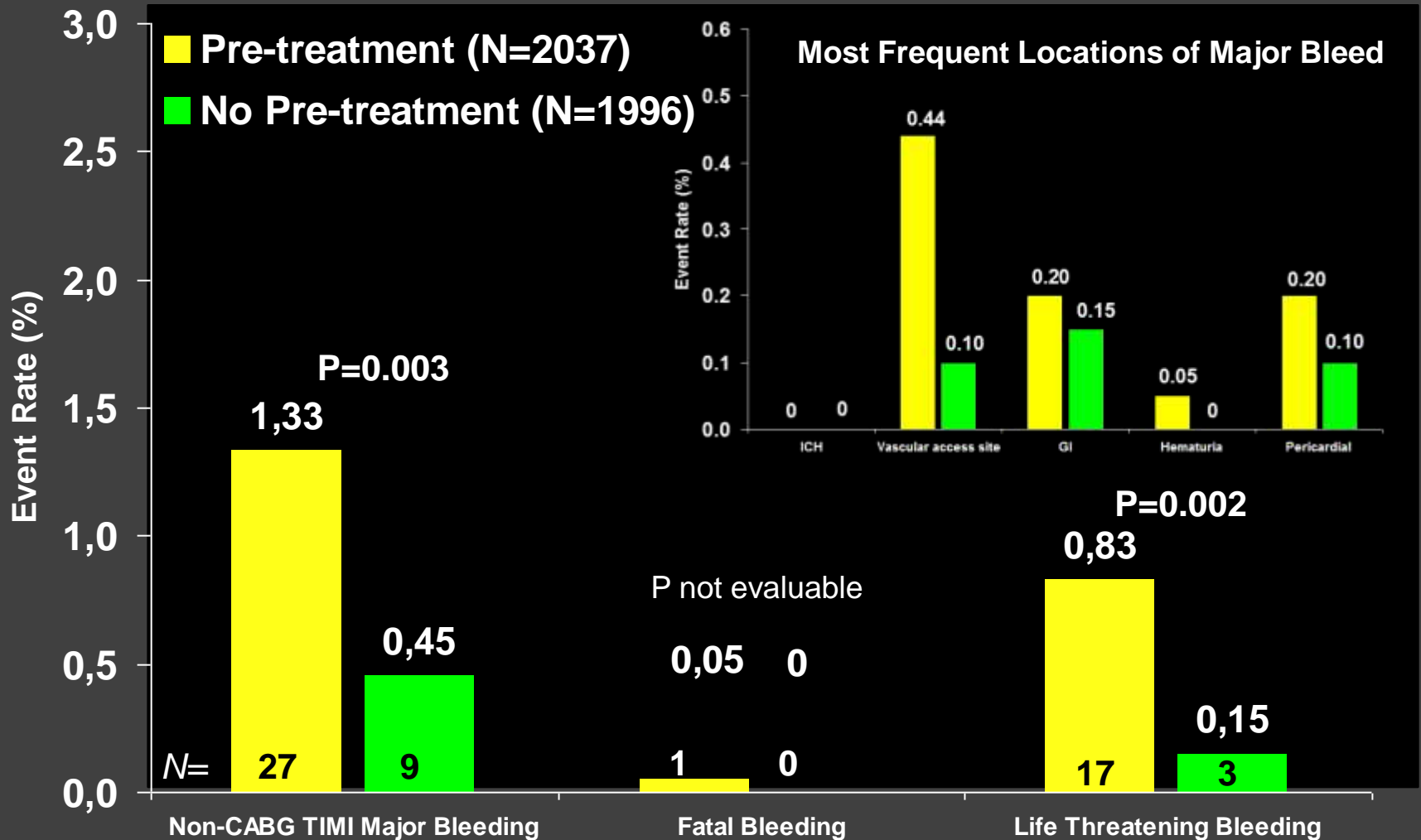
No. at Risk, All TIMI
Major Bleeding:

No pre-treatment	1996	1947	1328	1297	1288	1284	1263
Pre-treatment	2037	1972	1339	1310	1299	1297	1280

No pre-treatment	1996	1947	1328	1297	1288	1284	1263
Pre-treatment	2037	1972	1339	1310	1299	1297	1280

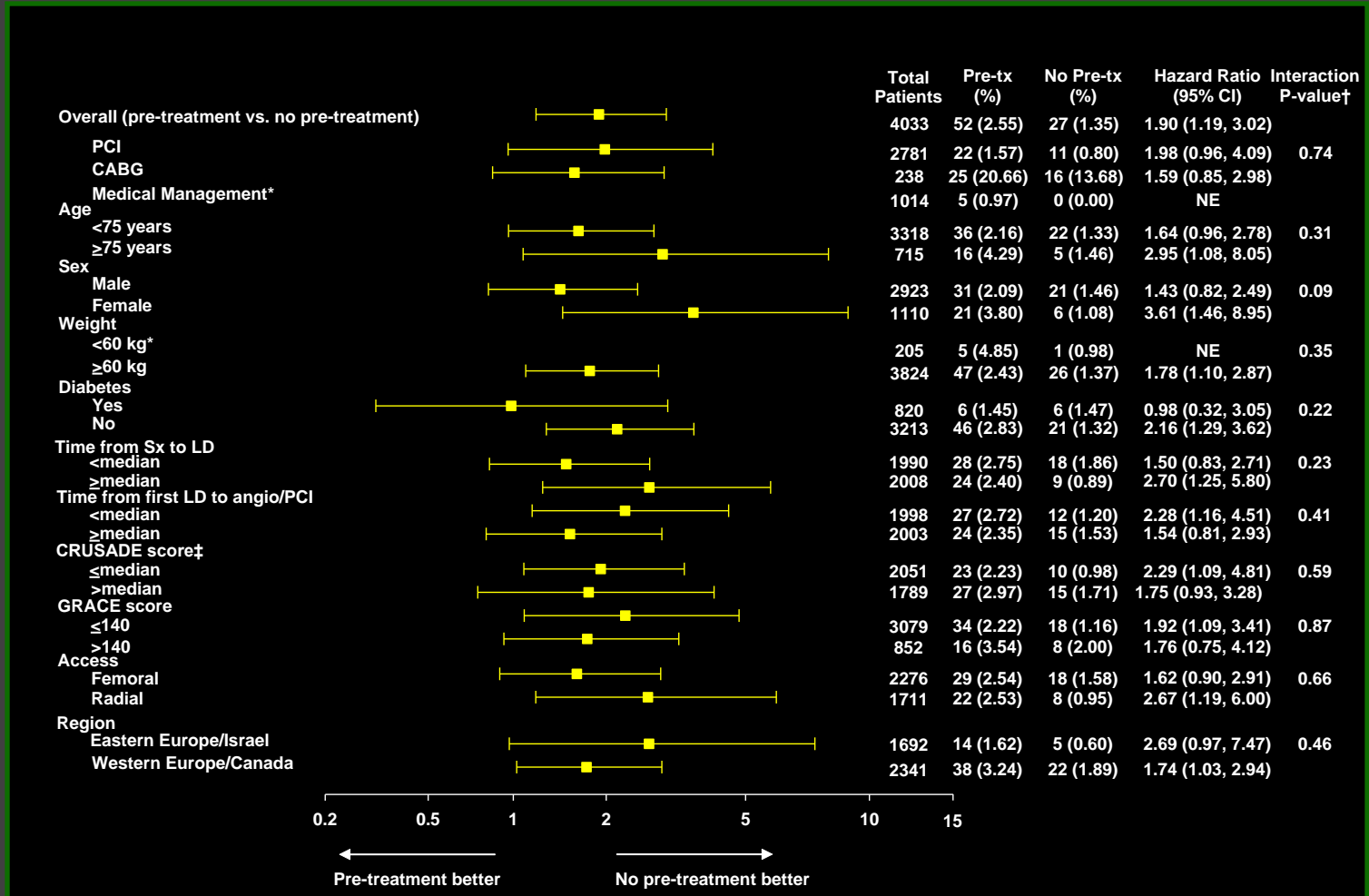


Non-CABG TIMI Major Bleeding Endpoints Through 7 Days (All Treated Patients)





All TIMI Major Bleeding for Prespecified Subgroups Through 7 days (All Treated Patients)



*Hazard ratio not evaluated for <10 events.

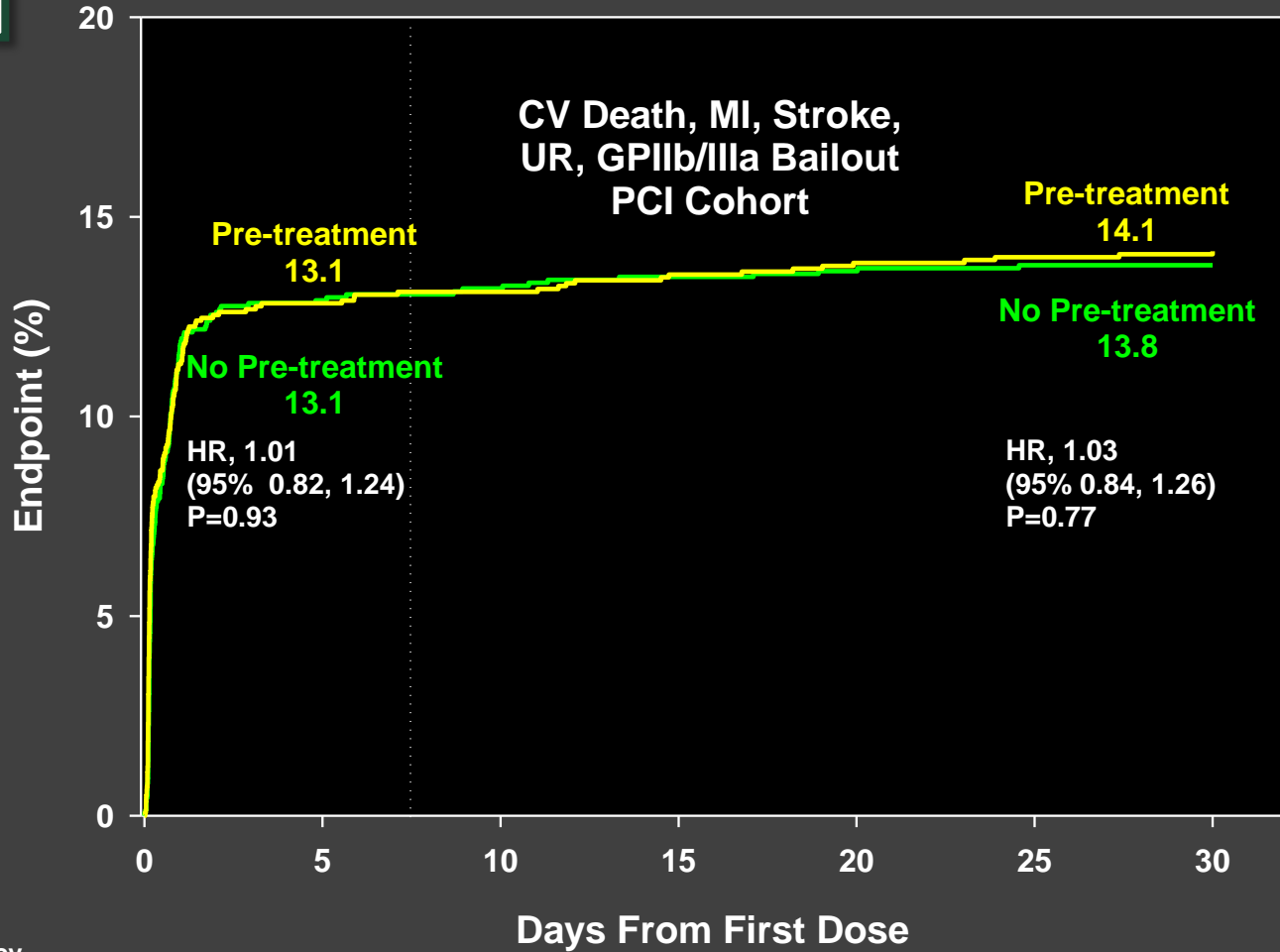
†Interaction p-value is from a Cox proportional hazards model with treatment, subgroup, and the treatment-by-subgroup interaction as fixed effects; ‡CRUSADE score is a post-hoc analysis; PCI includes 11 patients with PCI + CABG.



ACCOAST PCI



1° Efficacy Endpoint (PCI Patients)

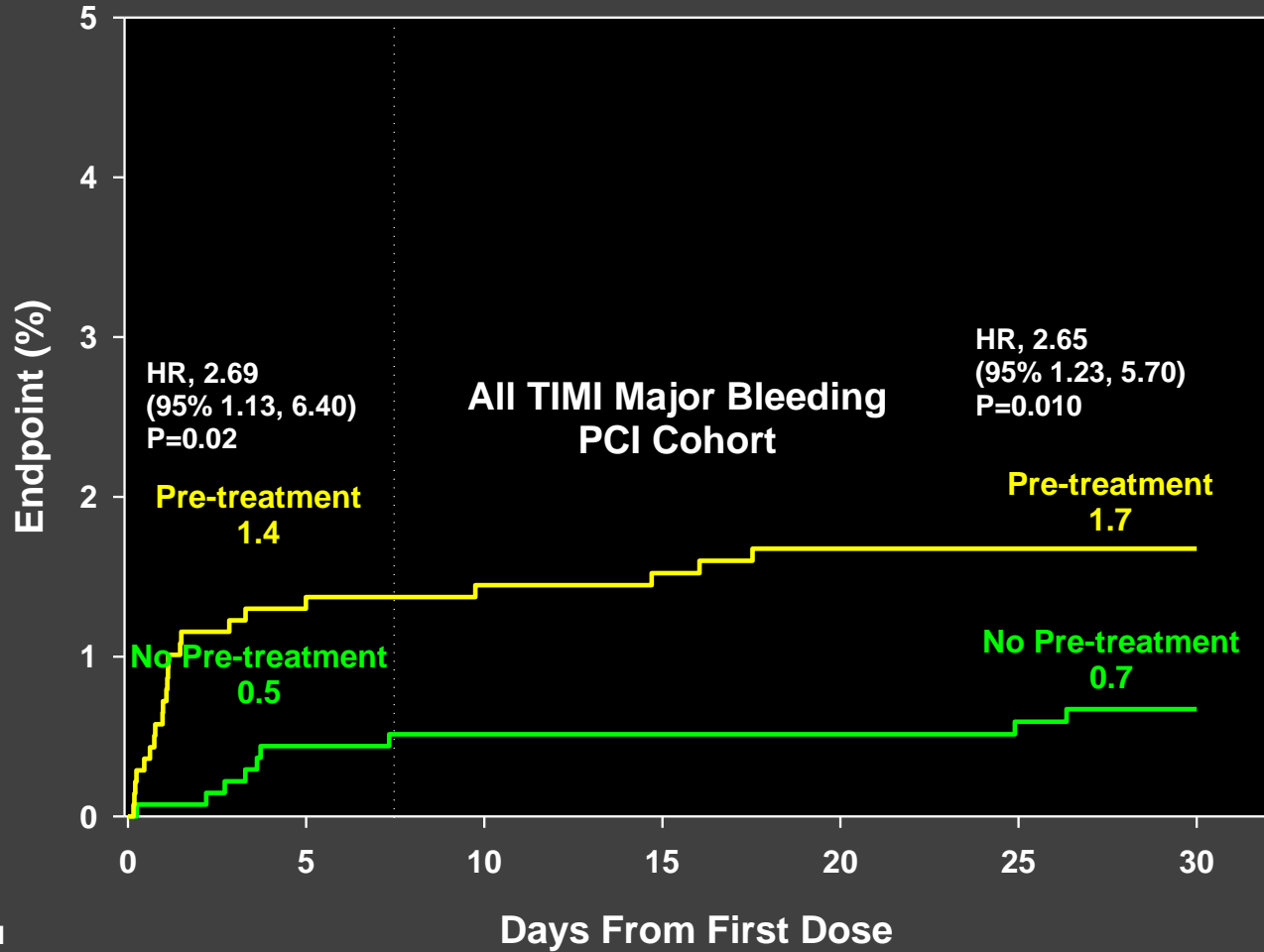


No. at Risk, Efficacy
End Point:

No pre-treatment	1372	1191	1187	1183	1179	1177	1177
Pre-treatment	1389	1206	1202	1194	1189	1186	1172



All TIMI Major Bleeding (PCI Patients)



No. at Risk, All TIMI
Major Bleeding:

No pre-treatment

1372
1389

1356
1364

1302
1314

1280
1293

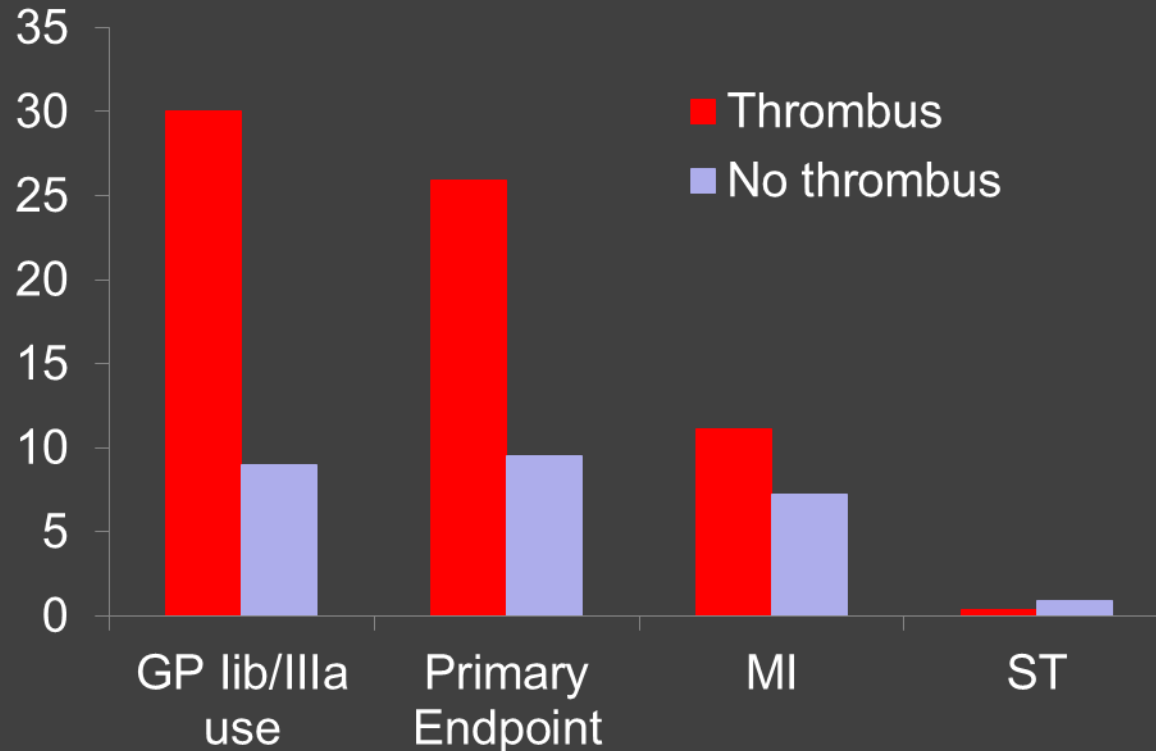
1272
1282

1268
1280

1249
1269



Impact of Visible thrombus



HR 2.61 [2.09-3.25], $p < 0.001$

-Length of procedure (HR: 1.88 (1.49, 2.36) $p < 0.001$,

-number of lesions (HR: 1.24 (1.10, 1.39) $p < 0.001$,

-maximum length of stent (HR: 1.19 (1.04, 1.35) $p = 0.005$),

-and CRUSADE risk score (HR: 1.01 (1.00, 1.02) $p = 0.023$;

CONCLUSIONS

ACCOAST

- In NSTEMI-ACS invasively managed <48 hours of admission, pre-treatment with prasugrel does not reduce MACE at but increases major bleedings.
- The results are consistent among patients undergoing PCI supporting treatment with prasugrel once the coronary anatomy has been defined.
- No subgroup appears to have a favorable risk/benefit ratio of pre-treatment.
- Reappraisal of routine pre-treatment strategies in NSTEMI-ACS is needed.

ACCOAST-PCI

- Reinforces the role the angiogram to ascertain the diagnosis of NSTEMI,
- Shows no downside in waiting for the coronary angiogram in patients who will need DAPT for stenting.
- Shows that angiogram provides additional information on the risk of the procedure and the prognosis
- Demonstrates that prasugrel loading after angiogram is not only safer but also effective in this population
- Such strategy gives flexibility and no bleeding risk

NSTEMI

↓ Aspirin 500 mg IV
Enox SQ

Fast transfer to the cathlab (24h) with TNI+
or high-risk features*

NO

YES

Ticagrelor

Clopidogrel

↓
Cath

↓
Cath

↓
Treatment on the table
with prasugrel

* At the exclusion of STEMI-like