ACUITY

A Prospective, Randomized Trial of Bivalirudin in Acute Coronary Syndromes

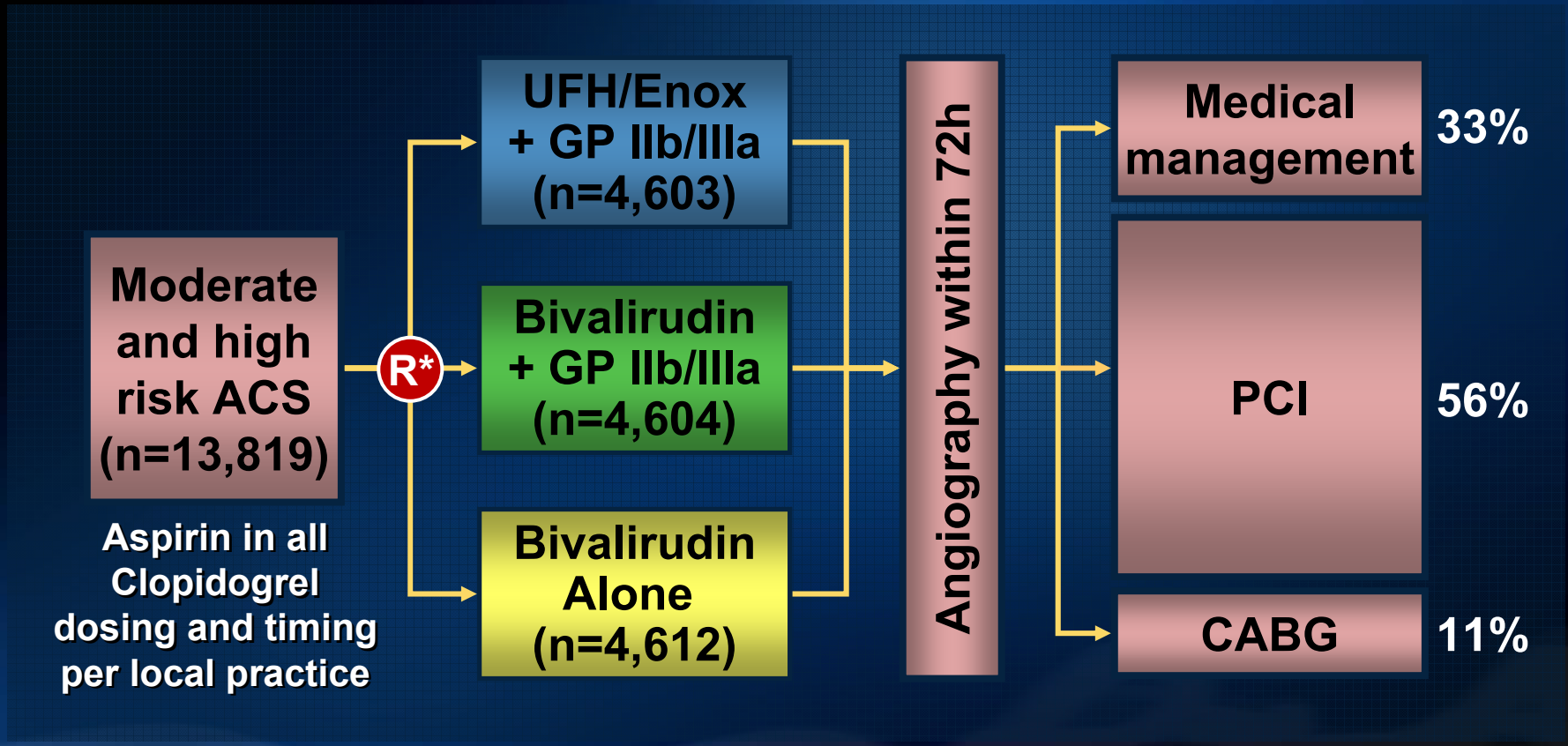
Final One-Year Results from the ACUITY Trial

Roxana Mehran MD
Gregg W. Stone MD-PI
for the ACUITY Investigators

ACUITY

Study Design – First Randomization

Moderate and high risk unstable angina or NSTEMI undergoing an invasive strategy (N = 13,819)

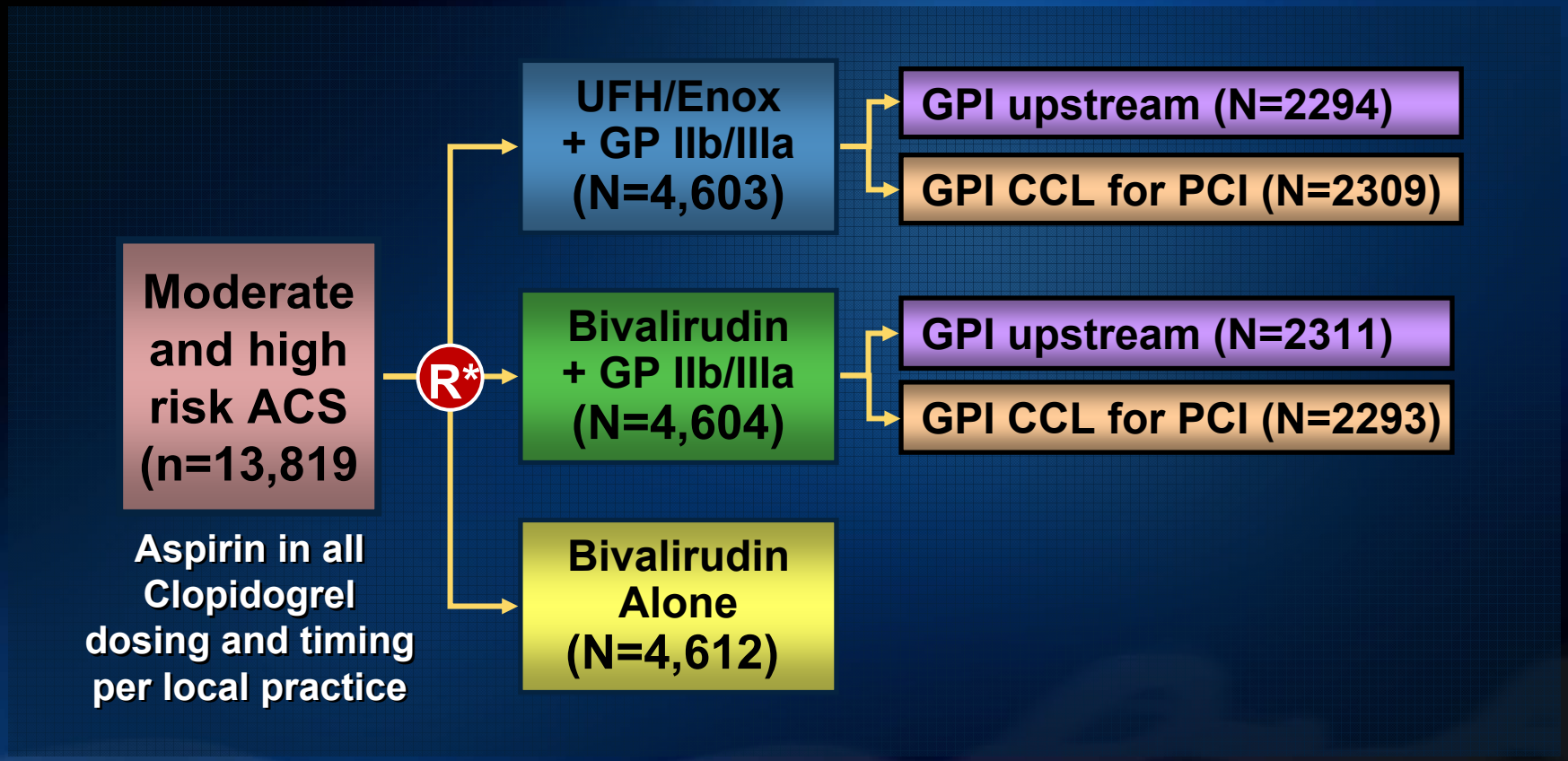


*Stratified by pre-angiography thienopyridine use or administration

ACUITY

Study Design – Second Randomization

Moderate and high risk unstable angina or NSTEMI undergoing an invasive strategy (N = 13,819)



*Stratified by pre-angiography thienopyridine use or administration

ACUITY

Baseline Characteristics

	UFH/Enoxaparin + GP IIb/IIIa (N=4,603)	Bivalirudin + GP IIb/IIIa (N=4,604)	Bivalirudin alone (N=4,612)
Age (median [range], yrs)	63 [23-91]	63 [21-95]	63 [20-92]
Male	70.6%	69.9%	69.3%
Weight (median [IQR], kg)	83 [73-95]	83 [73-95]	84 [73-96]
Diabetes	28.5%	27.8%	28.1%
- Insulin requiring	8.5%	8.7%	8.9%
Hypertension	66.8%	67.2%	67.1%
Hyperlipidemia	57.2%	57.4%	57.0%
Current smoker	29.0%	29.3%	29.0%
Prior MI	31.6%	30.5%	31.8%
Prior PCI	38.9%	37.8%	39.9%
Prior CABG	18.2%	17.4%	18.1%
Renal insufficiency*	19.2%	19.2%	18.9%

* creatinine clearance <60 mL/min

ACUITY

Baseline High Risk Features

	UFH/Enoxaparin + GP IIb/IIIa (N=4,603)	Bivalirudin + GP IIb/IIIa (N=4,604)	Bivalirudin alone (N=4,612)
Biomarker or ST Δ	73.1%	71.6%	72.4%
- Biomarker +	59.4%	58.6%	60.3%
- Troponin +	58.3%	57.2%	59.2%
- ST-segment Δ	35.2%	35.4%	34.3%
TIMI Risk Score†			
- 0-2*	16.1%	15.4%	15.6%
- 3-4	53.7%	55.5%	54.5%
- 5-7	30.3%	29.1%	29.9%

*80.1% were biomarker+ or had baseline STΔ

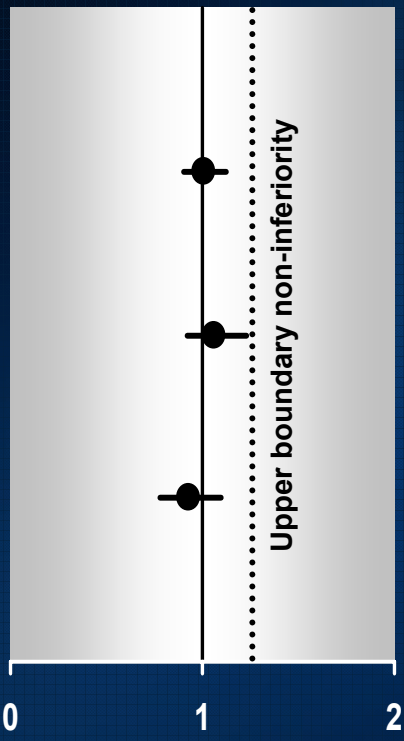
†97% were TIMI intermediate or high risk, or biomarker+, or +STΔ

ACUITY

Primary Endpoint Measures (ITT) – 30 Days

UFH/Enoxaparin + GPI vs. Bivalirudin + GPI

Primary endpoint	Bival + IIb/IIIa	UFH/Enox + IIb/IIIa	RR (95% CI)	p value (non inferior) (superior)
Net clinical outcome	11.8%	11.7%	1.01 (0.90-1.12)	<0.001 0.93
Ischemic composite	7.7%	7.3%	1.07 (0.92-1.23)	0.015 0.39
Major bleeding	5.3%	5.7%	0.93 (0.78-1.10)	<0.001 0.38



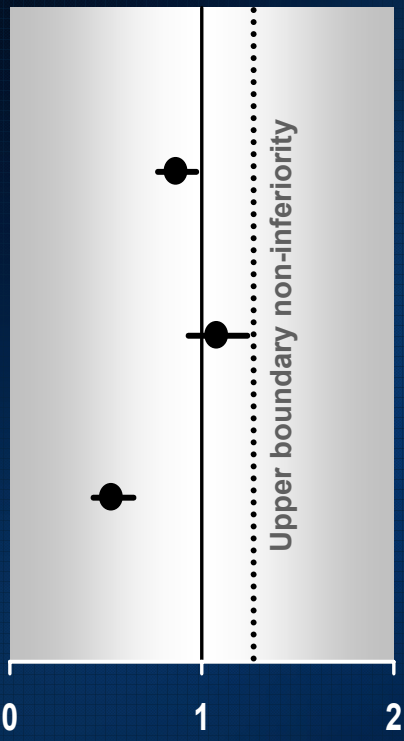
Stone GW et al. NEJM 2006;355:2203-16

ACUITY

Primary Endpoint Measures (ITT) – 30 Days

UFH/Enoxaparin + GPI vs. Bivalirudin Alone

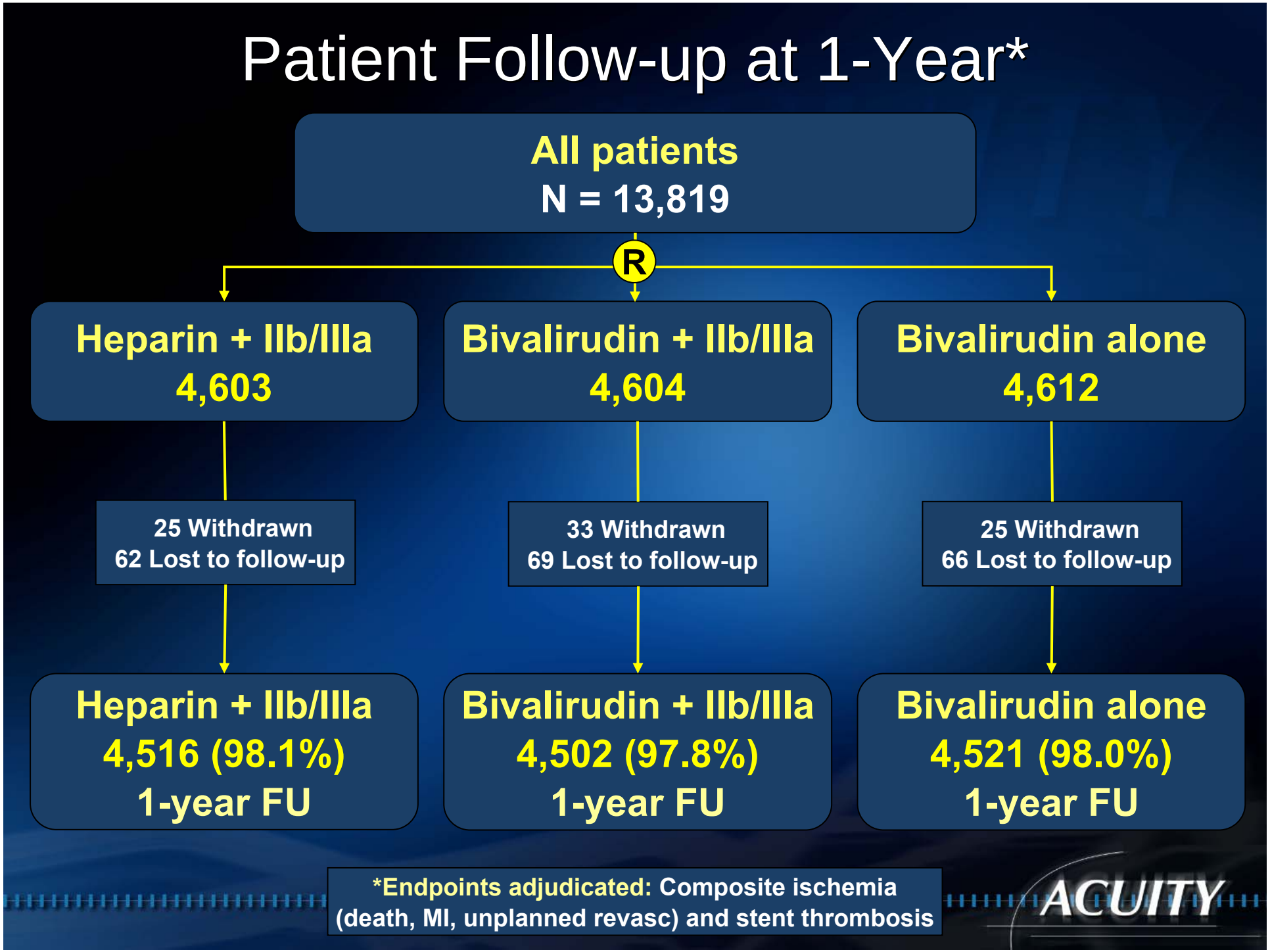
Primary endpoint	Bival alone	UFH/Enox + IIb/IIIa	RR (95% CI)	p value (non inferior) (superior)
Net clinical outcome	10.1%	11.7%	0.86 (0.77-0.97)	<0.001 0.015
Ischemic composite	7.8%	7.3%	1.08 (0.93-1.24)	0.01 0.32
Major bleeding	3.0%	5.7%	0.53 (0.43-0.65)	<0.001 <0.001



Stone GW et al. NEJM 2006;355:2203-16

ACUITY

Patient Follow-up at 1-Year*



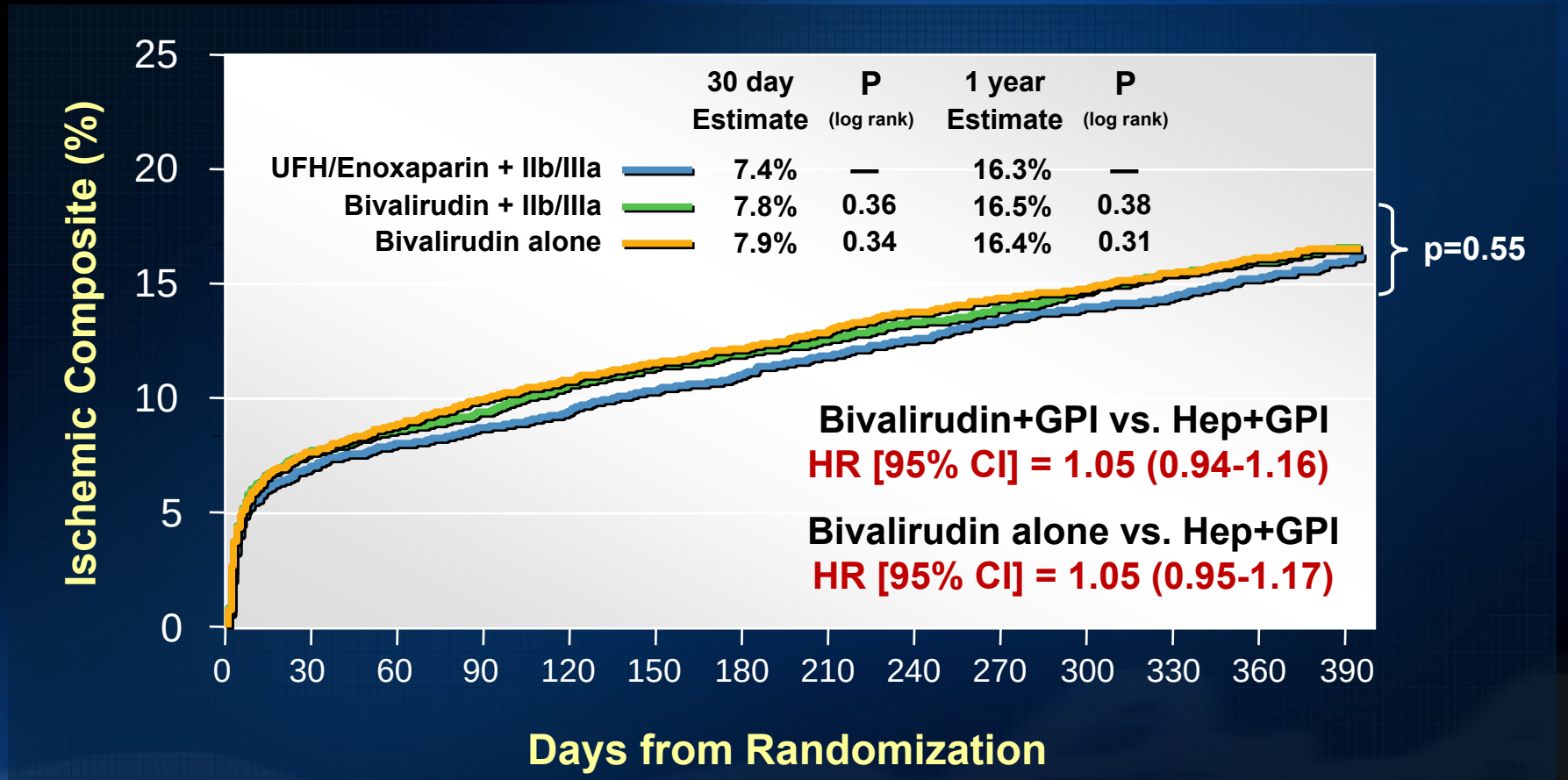
*Endpoints adjudicated: Composite ischemia (death, MI, unplanned revasc) and stent thrombosis

ACUITY

Ischemic Composite Endpoint

(Death, MI, unplanned revascularization for ischemia)

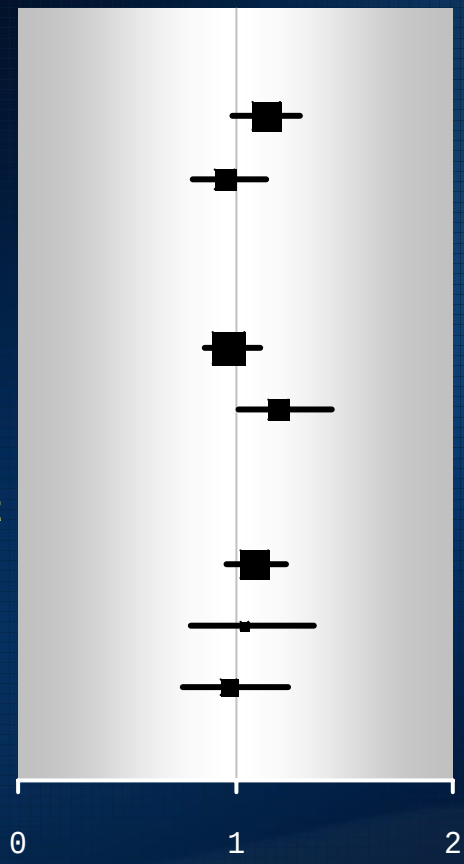
UFH/Enoxaparin + GPI vs. Bivalirudin + GPI vs. Bivalirudin Alone



ACUITY

Composite Ischemia at 1-Year

UFH/Enoxaparin + GPIIb/IIIa vs. Bivalirudin alone

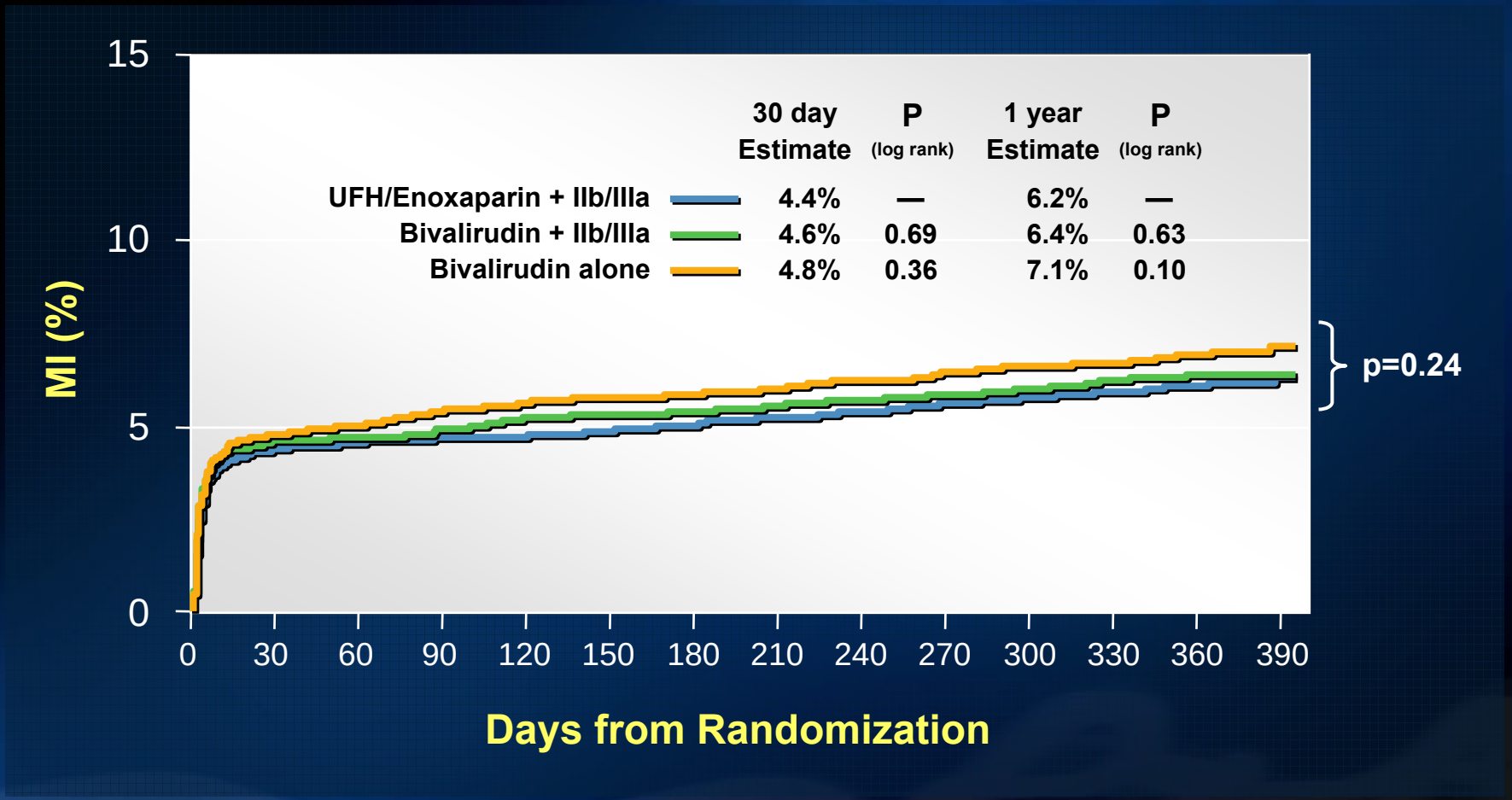


	1 yr KM estimate Bival alone	UFH/Enox + IIb/IIIa	HR (95% CI)	P_{int}
Biomarkers (CK/Trop)				
Elevated (n=5072)	17.7%	16.4%	1.14 (0.99-1.30)	0.11
Normal (n=3402)	14.6%	16.1%	0.95 (0.80-1.14)	
Pre Thienopyridine				
Yes (n=5751)	16.2%	17.2%	0.97 (0.86-1.11)	0.07
No (n=3305)	16.4%	14.3%	1.20 (1.01-1.44)	
Actual Treatment				
PCI (n=5179)	19.8%	19.2%	1.09 (0.96-1.23)	
CABG (n=1040)	21.1%	20.7%	1.04 (0.79-1.36)	0.67
Medical (n=2994)	9.0%	9.6%	0.97 (0.76-1.24)	

ACUITY

Myocardial Infarction

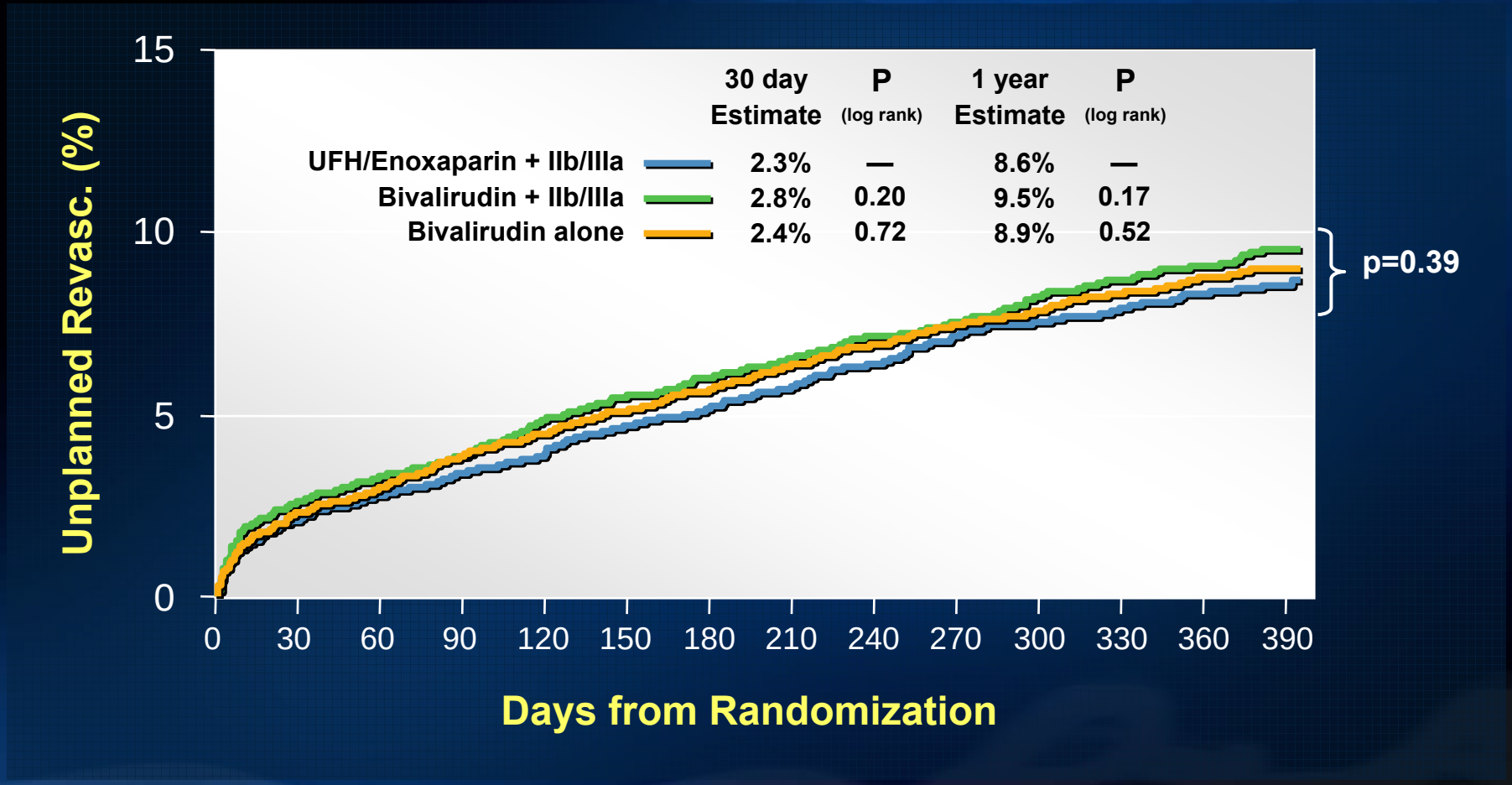
UFH/Enoxaparin + GPI vs. Bivalirudin + GPI vs. Bivalirudin Alone



ACUITY

Unplanned Revascularization

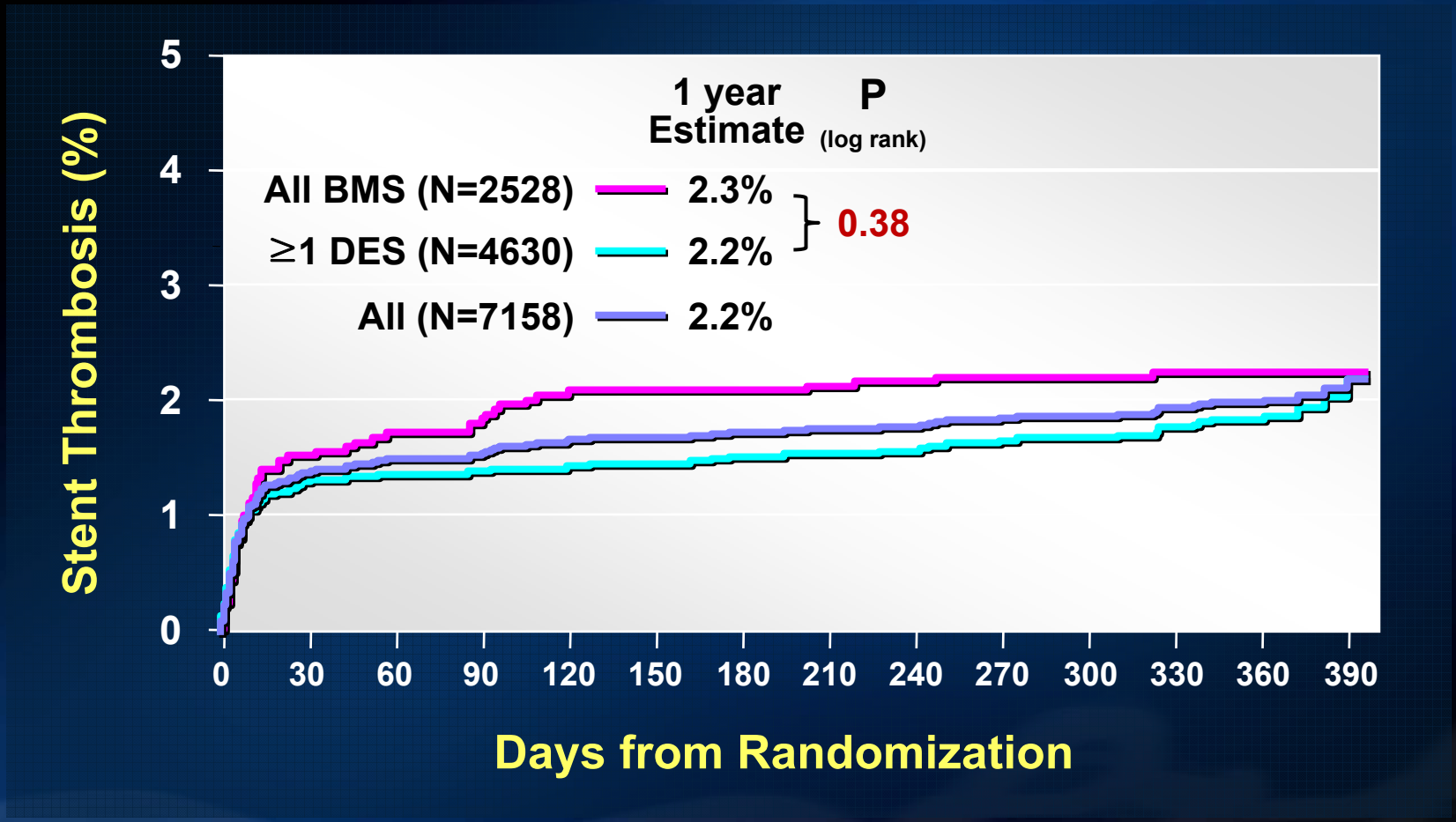
UFH/Enoxaparin + GPI vs. Bivalirudin + GPI vs. Bivalirudin Alone



ACUITY

Stent Thrombosis (Protocol Defn.)

Drug-eluting Stents (DES) vs. Bare Metal Stents (BMS)



ACUITY

Stent Thrombosis (Protocol): Definite/Probable

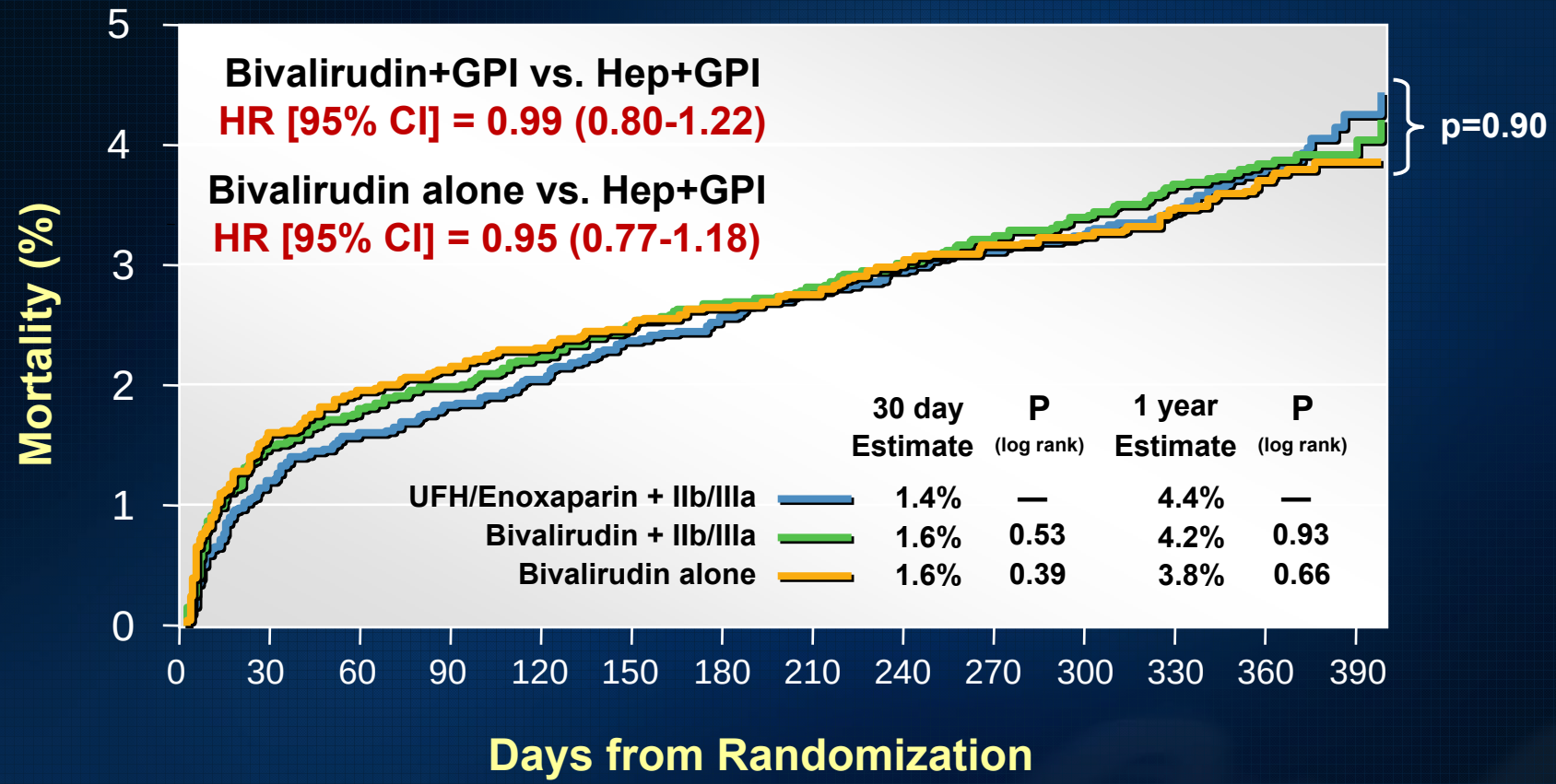
	UFH/Enoxaparin + GP IIb/IIIa (N=2348)	Bivalirudin + GP IIb/IIIa (N=2403)	Bivalirudin alone (N=2407)	P_1 Value	P_2 Value
Total-all stent pts	**2.3%**	**2.4%**	**1.9%**	0.38	0.74
▪ 0 – 30 days	1.3%	1.6%	1.3%	0.39	0.97
▪ 30 days – 1 year	1.0%	0.8%	0.5%	0.78	0.52
Total – at least one DES implanted	**2.5%**	**2.4%**	**1.8%**	0.44	0.89
• 0 – 30 days	1.2%	1.6%	1.2%	0.28	0.87
• 30 days – 1 year	1.3%	0.7%	0.6%	0.82	0.64
Total – only BMS implanted	**2.3%**	**2.6%**	**2.0%**	0.69	0.71
• 0 – 30 days	1.6%	1.6%	1.5%	>0.99	0.87
• 30 days – 1 year	0.6%	1.0%	0.5%	0.49	0.65

ACUITY

P_1 = Bivalirudin+GPI vs. UFH/Enox+GPI; P_2 = Bivalirudin alone vs. UFH/Enox+GPI

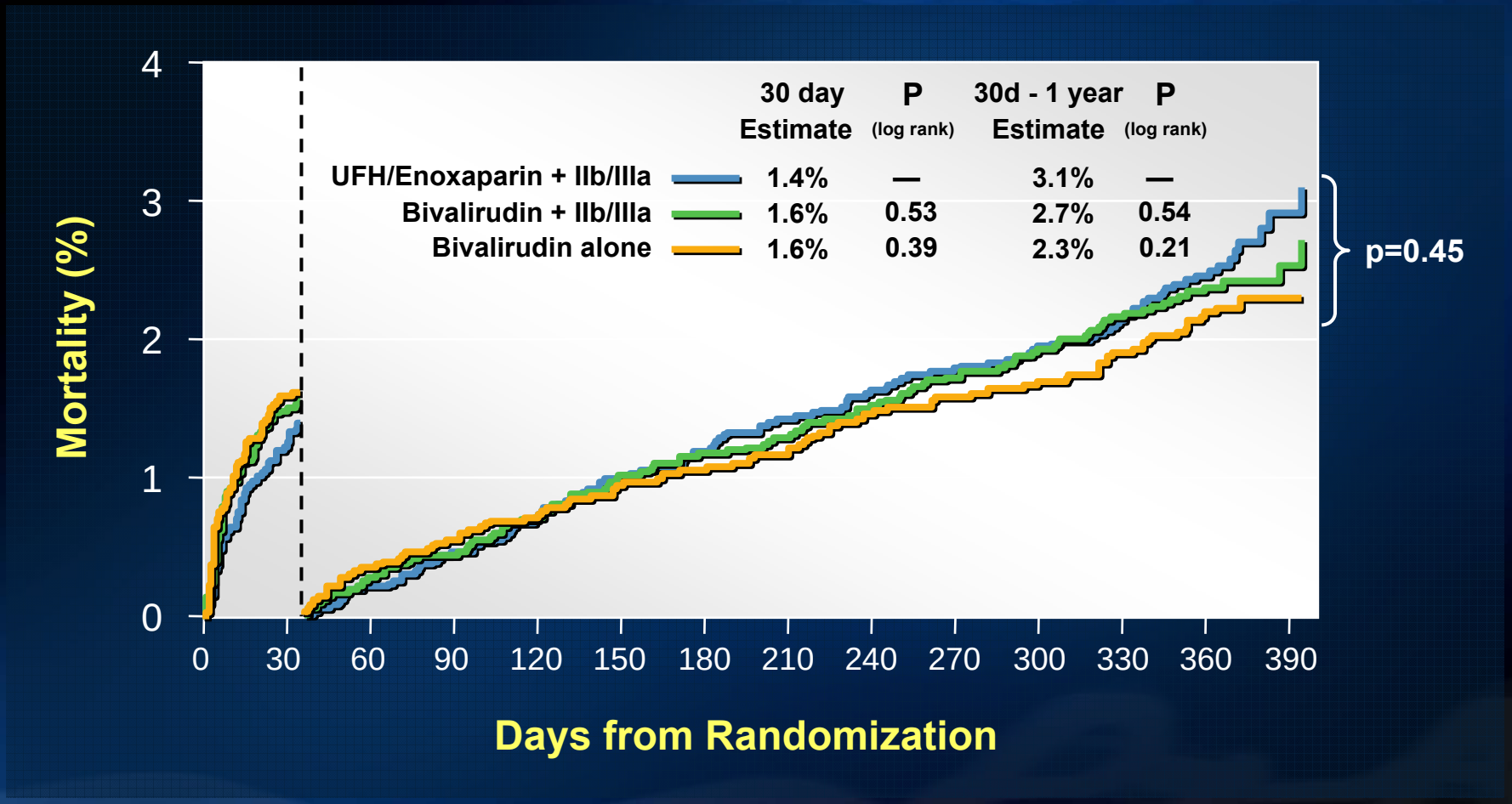
Mortality: 524 total deaths at 1-year

UFH/Enoxaparin + GPI vs. Bivalirudin + GPI vs. Bivalirudin Alone



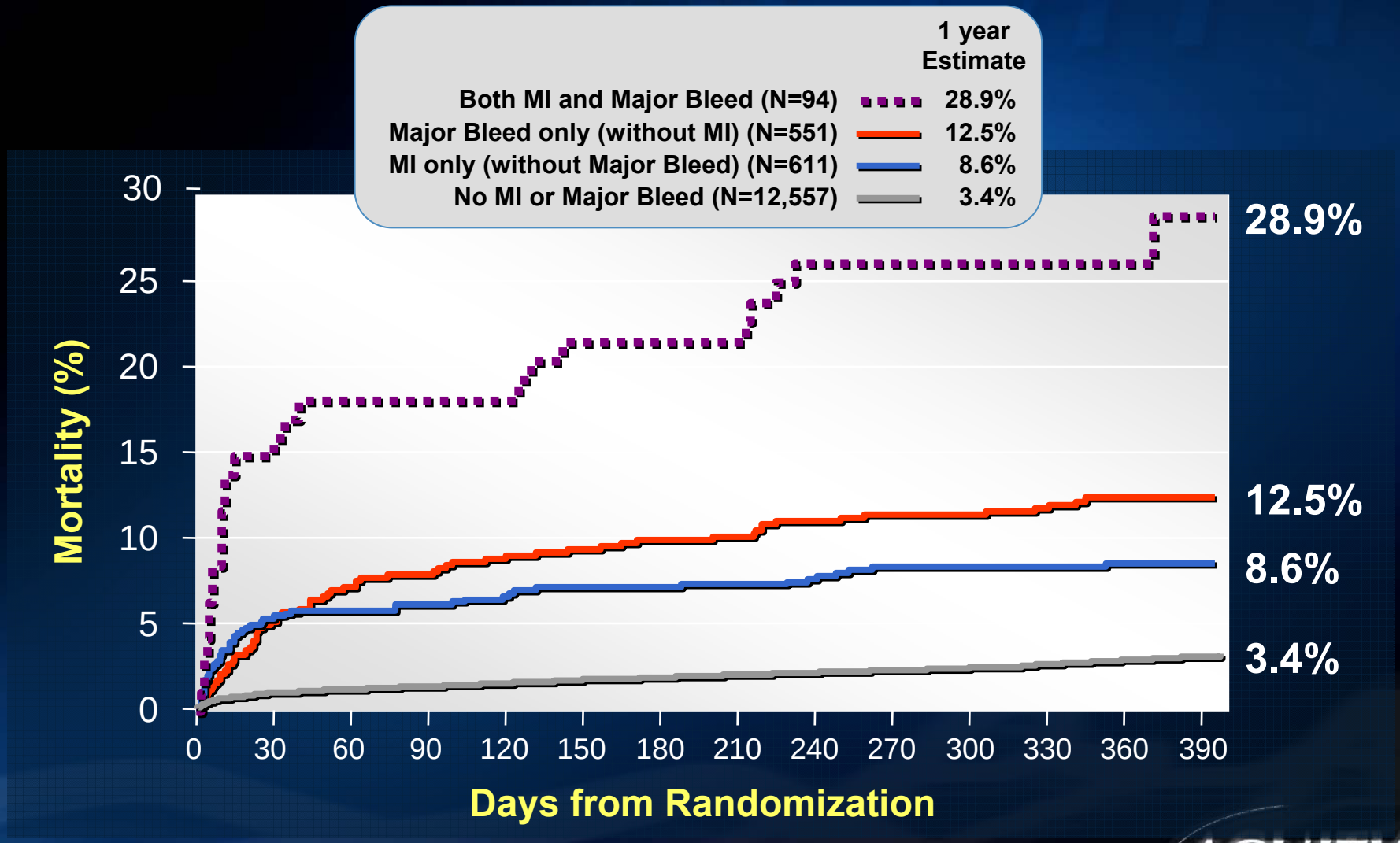
ACUITY

Early and Late Mortality
Landmark analysis



ACUITY

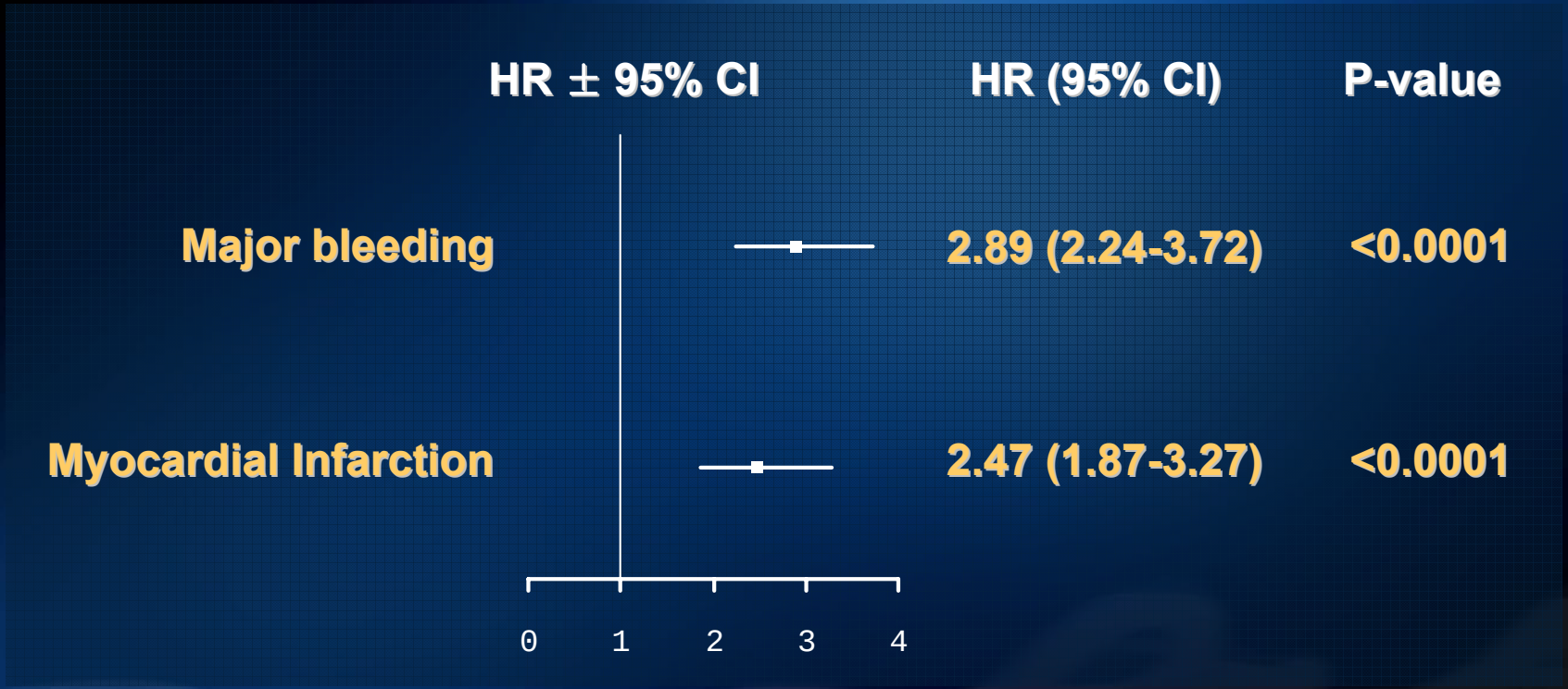
Impact of MI and Major Bleeding (non-CABG) in the First 30 Days on Risk of Death Over 1 Year



ACUITY

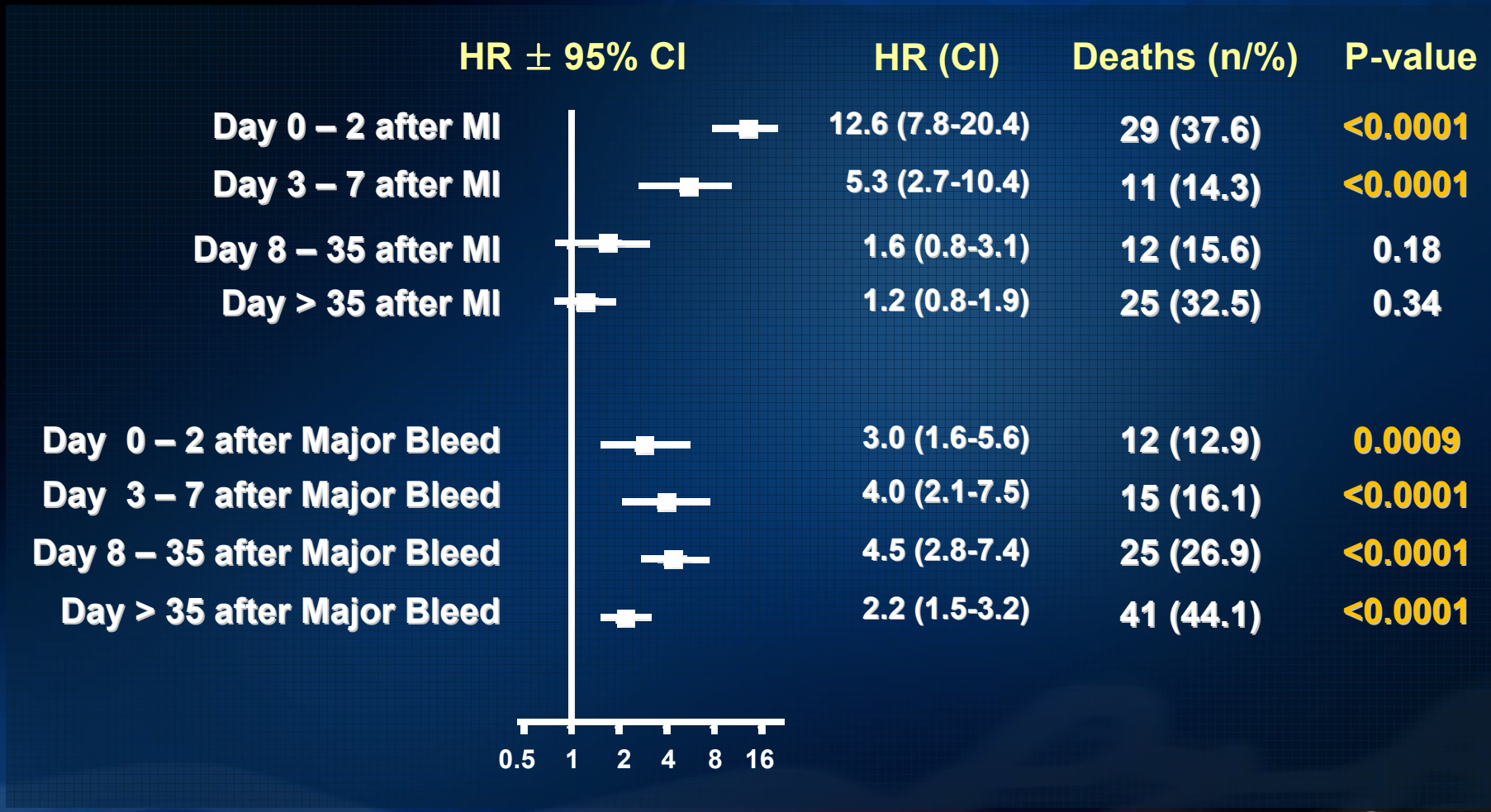
Influence of Major Bleeding and MI in the First 30 Days on Risk of Death Over 1 Year

Cox model adjusted for baseline predictors, with non-CABG major bleeding and MI as time-updated covariates



ACUITY

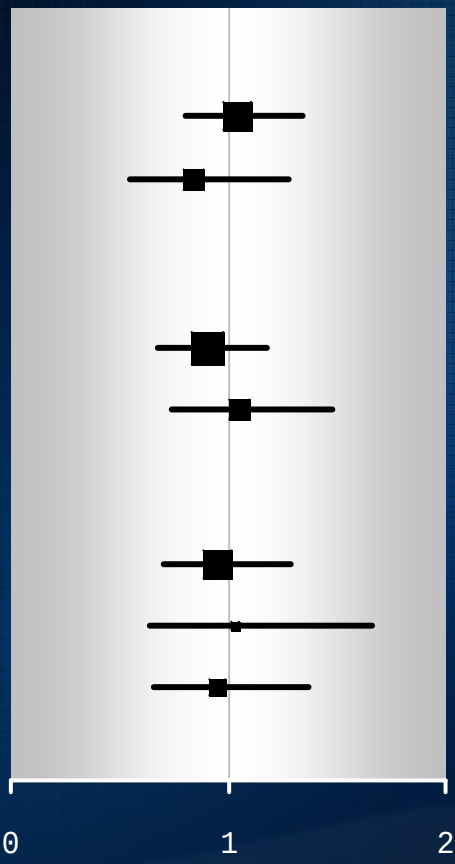
Influence of Non-CABG Major Bleeding and MI in the First 30 Days on the Risk of Death Over 1 Year



ACUITY

Death at 1-Year

UFH/Enoxaparin + GPIIb/IIIa vs. Bivalirudin alone



	Hazard ratio ±95% CI	1 yr KM estimate Bival alone	UFH/Enox + IIb/IIIa	HR (95% CI)	P_{int}
Biomarkers (CK/Trop)					
Elevated (n=5072)		4.8%	5.0%	1.04 (0.80-1.34)	0.40
Normal (n=3402)		2.4%	3.6%	0.84 (0.55-1.28)	
Pre Thienopyridine					
Yes (n=5751)		3.5%	4.2%	0.90 (0.68-1.18)	0.52
No (n=3305)		4.0%	4.4%	1.05 (0.74-1.48)	
Actual Treatment					
PCI (n=5179)		3.2%	4.0%	0.95 (0.70-1.29)	
CABG (n=1040)		6.8%	6.7%	1.03 (0.64-1.66)	0.96
Medical (n=2994)		4.0%	4.3%	0.95 (0.66-1.37)	

Bivalirudin alone better **UFH/Enox + IIb/IIIa better**

ACUITY

Conclusions

- In patients with moderate and high risk ACS undergoing an early invasive strategy with the use of GP IIb/IIIa inhibitors
  - Bivalirudin is an acceptable substitute for either unfractionated heparin or enoxaparin
- Compared to either UFH/enoxaparin with GP IIb/IIIa inhibitors *or* bivalirudin with GP IIb/IIIa inhibitors
  - A bivalirudin alone strategy results in marked reduction of bleeding at 30 days, and similar rates of mortality and composite ischemia at 1-year
- The results of this study further establish the important relationship between iatrogenic bleeding complications and mortality in patients with ACS

ACUITY