HORIZONS-AMI

A Prospective, Randomized Comparison of Bivalirudin vs. Heparin Plus Glycoprotein IIb/IIIa Inhibitors During Primary Angioplasty in Acute Myocardial Infarction

– One Year Results –

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For the HORIZONS-AMI Investigators

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Harmonizing Outcomes with Revascularization and Stents in AMI

3602 pts with STEMI with symptom onset ≤12 hours

Aspirin, thienopyridine

R
1:1

UFH + GP IIb/IIIa inhibitor (abciximab or eptifibatide)

Bivalirudin monotherapy (± provisional GP IIb/IIIa)

Pharmacology Arm
Primary and Secondary Endpoints
1-Year
Intention to Treat Population

Outcomes in the 4 randomized groups

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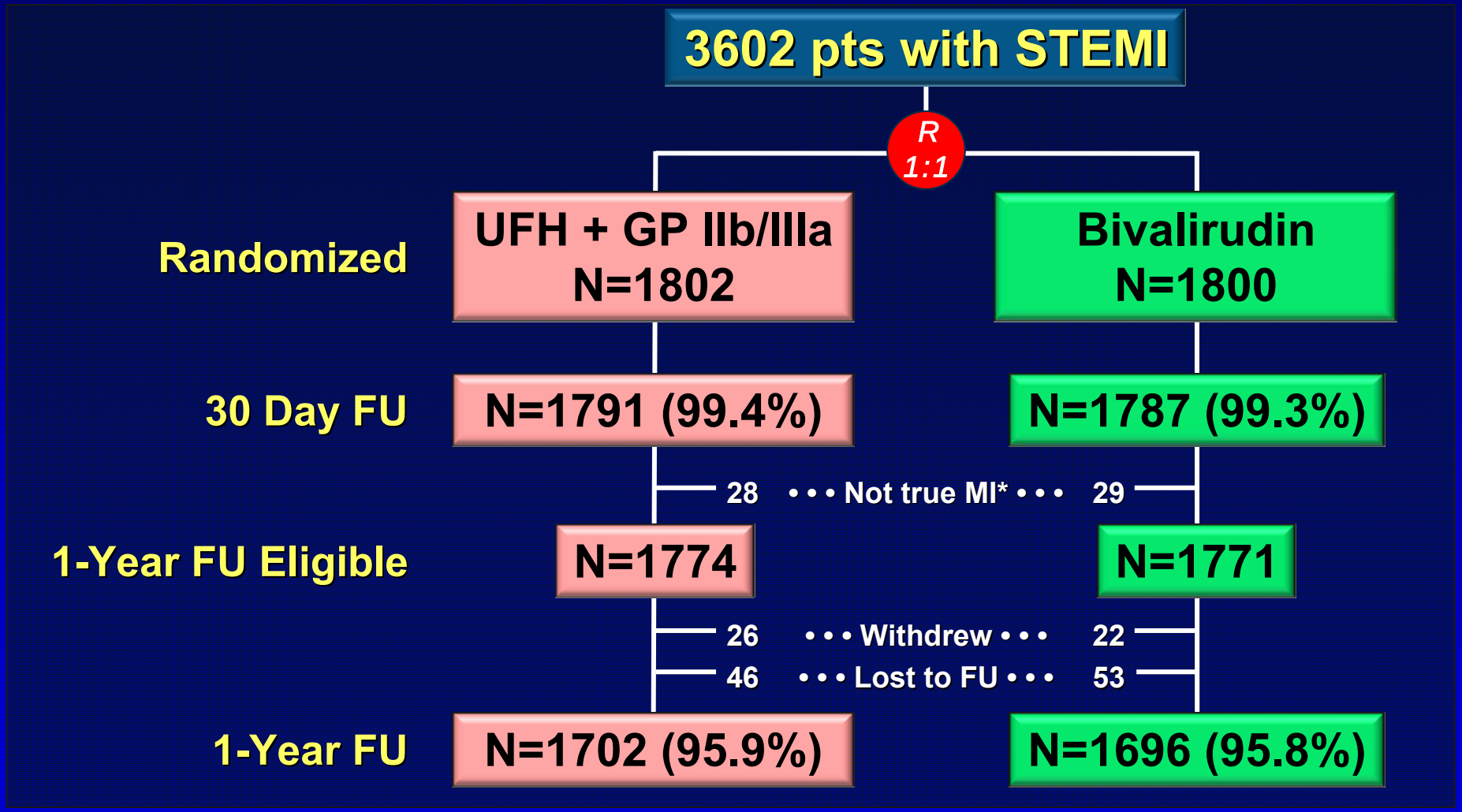
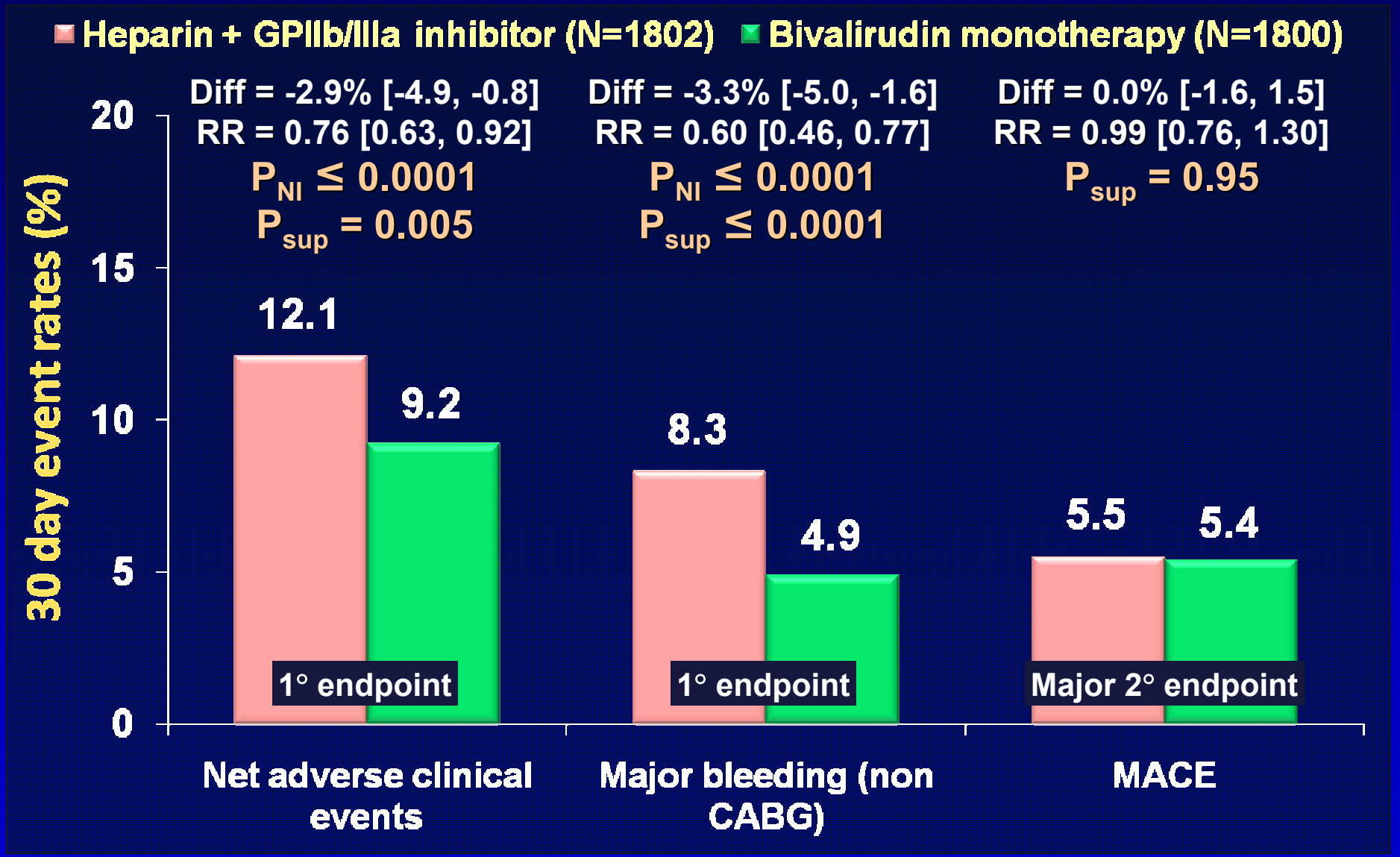


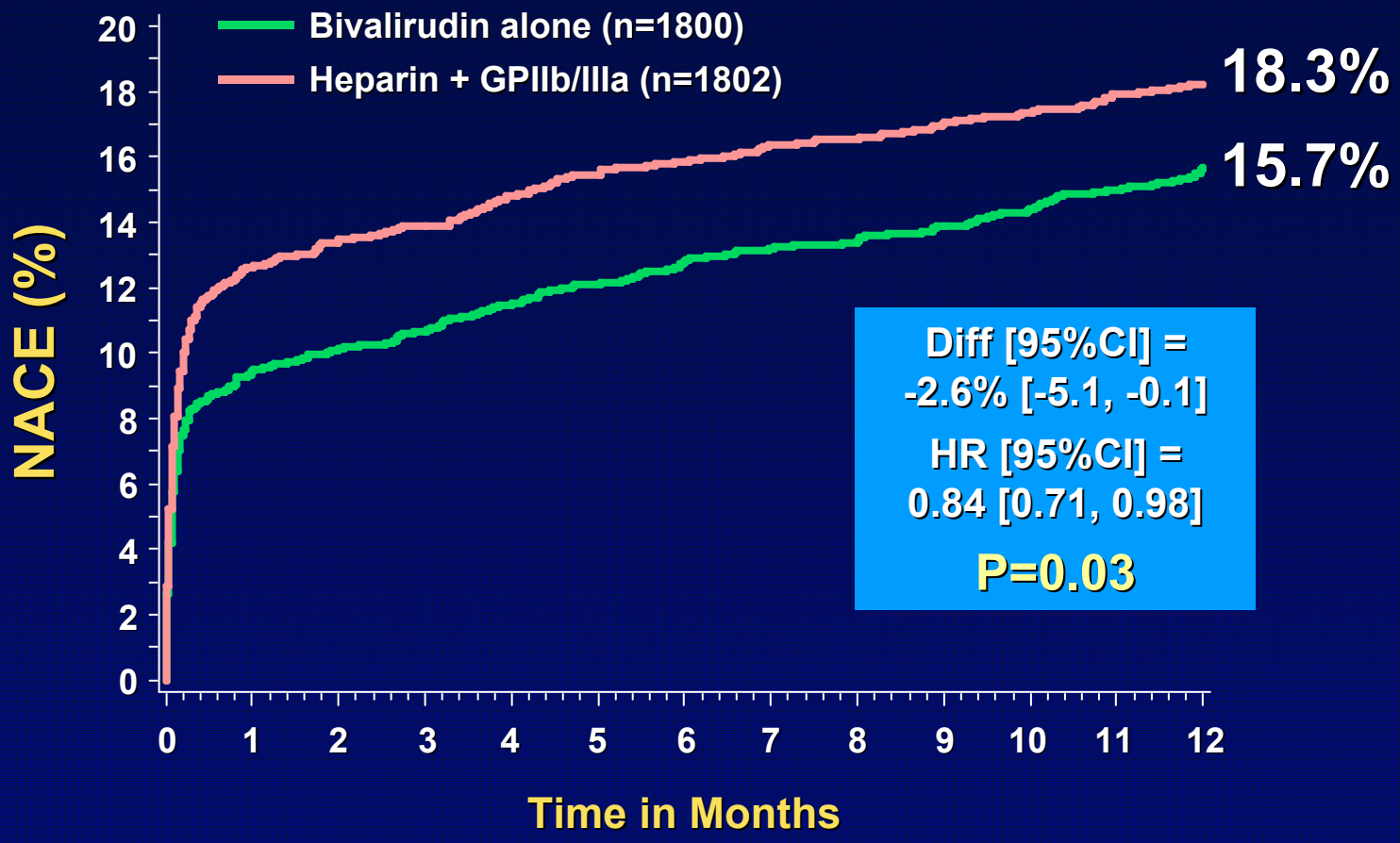
* Biomarkers WNL and no DS >50% by core lab determination → 30 day FU only

Primary Endpoints at 30 Days



Stone GW et al. NEJM 2008;358:2218-30

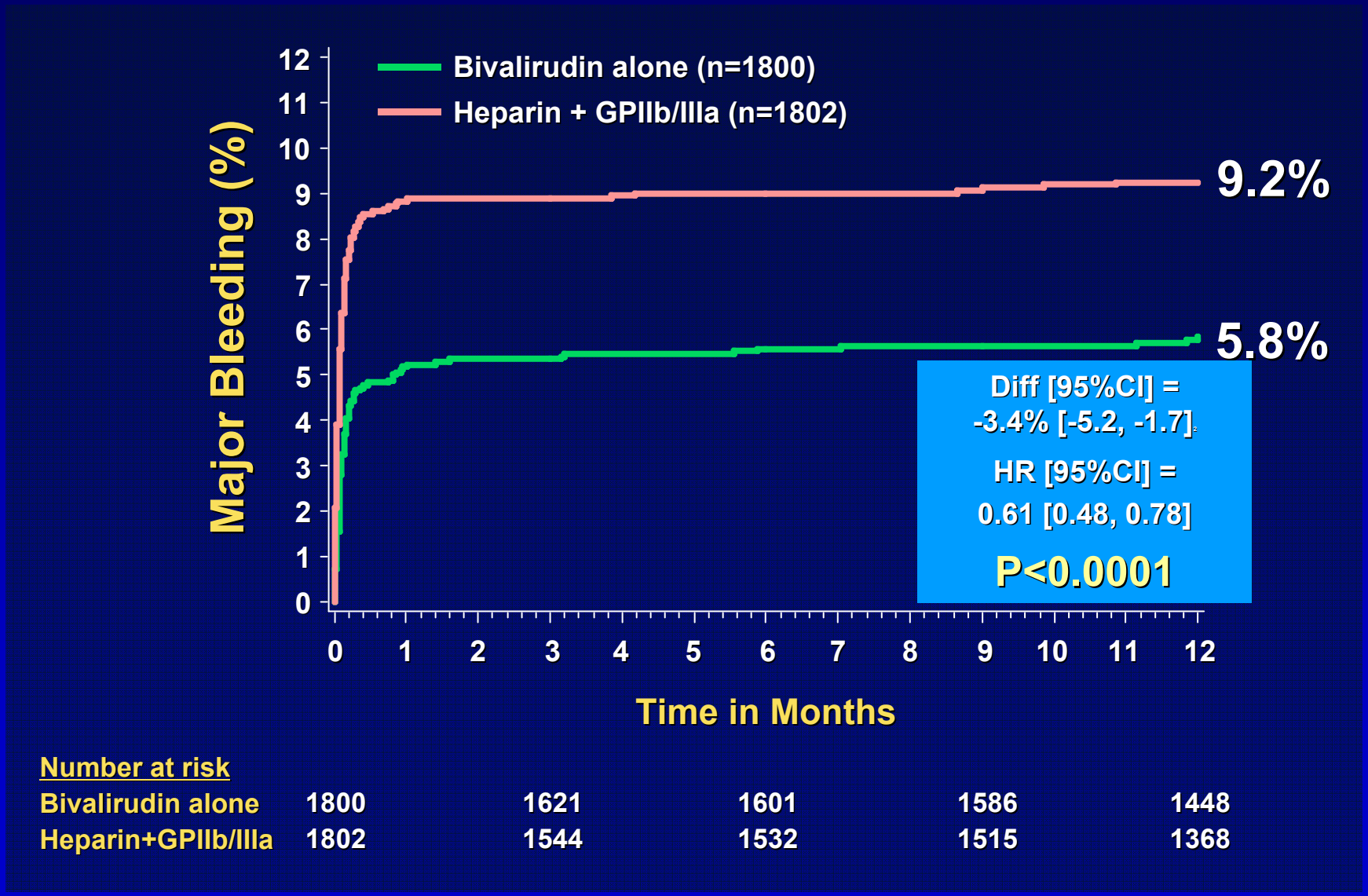
1-Year Net Adverse Clinical Events*



Number at risk					
Bivalirudin alone	1800	1559	1514	1483	1343
Heparin+GPIIb/IIIa	1802	1499	1459	1427	1281

*MACE or major bleeding (non CABG)

1-Year Major Bleeding (non-CABG)



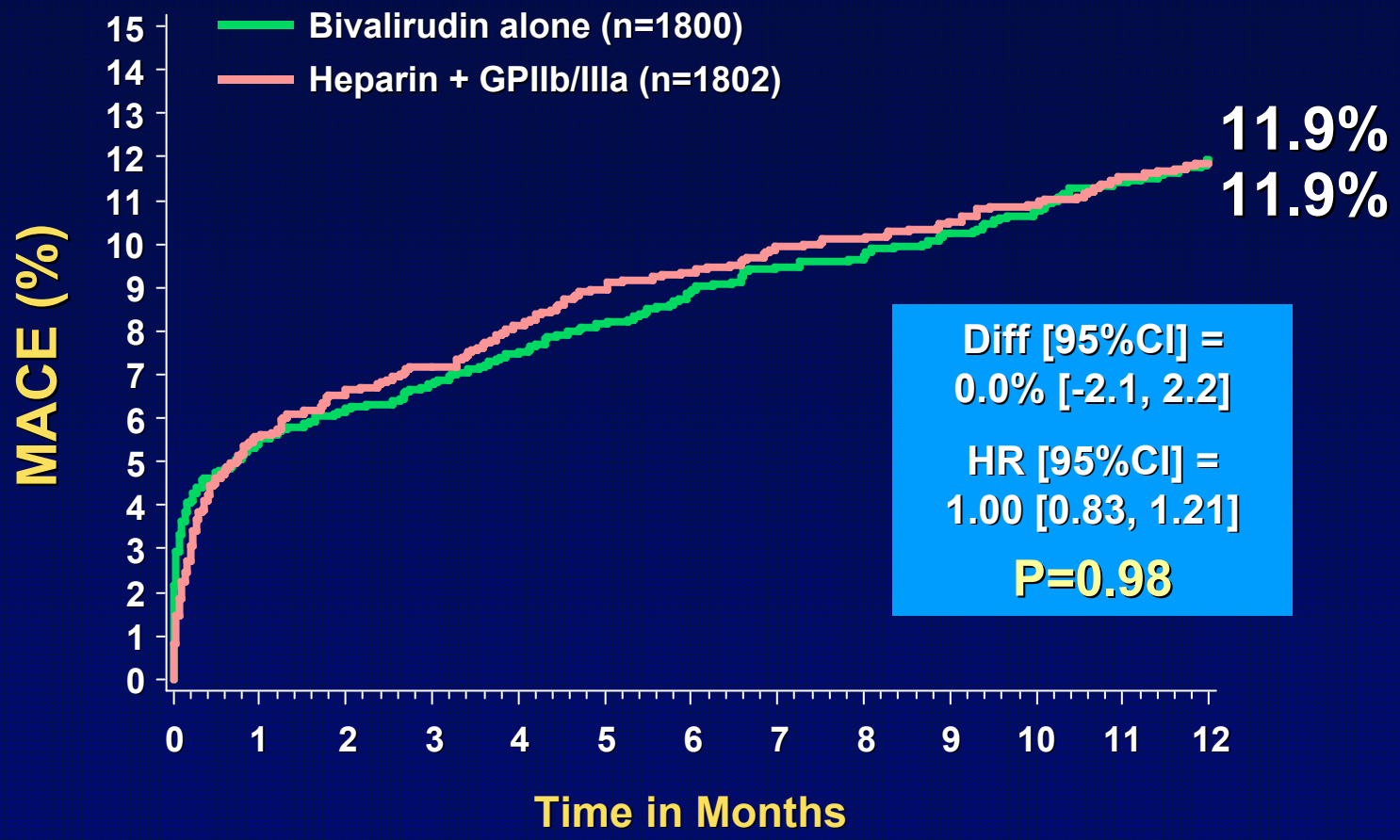
Number at risk					
Bivalirudin alone	1800	1621	1601	1586	1448
Heparin+GPIIb/IIIa	1802	1544	1532	1515	1368

1-Year Bleeding Endpoints*

	UFH + GP IIb/IIIa (N=1802)	Bivalirudin (N=1800)	P Value
Protocol Major, non CABG**	9.2%	5.8%	<0.0001
Protocol Major, All	11.8%	7.7%	<0.0001
Protocol Minor	16.5%	9.1%	<0.0001
Blood transfusion	4.0%	2.7%	0.02
TIMI Major	5.5%	3.6%	0.005
TIMI Minor	4.8%	3.0%	0.008
TIMI Major or Minor	10.2%	6.5%	<0.0001
GUSTO LT*** or Severe	0.7%	0.8%	0.70
GUSTO Moderate	5.4%	3.7%	0.01
GUSTO LT or Sev or Mod	6.0%	4.4%	0.02

*Kaplan-Meier estimates; all CEC adjudicated, except protocol minor;
**Primary endpoint; ***Life threatening

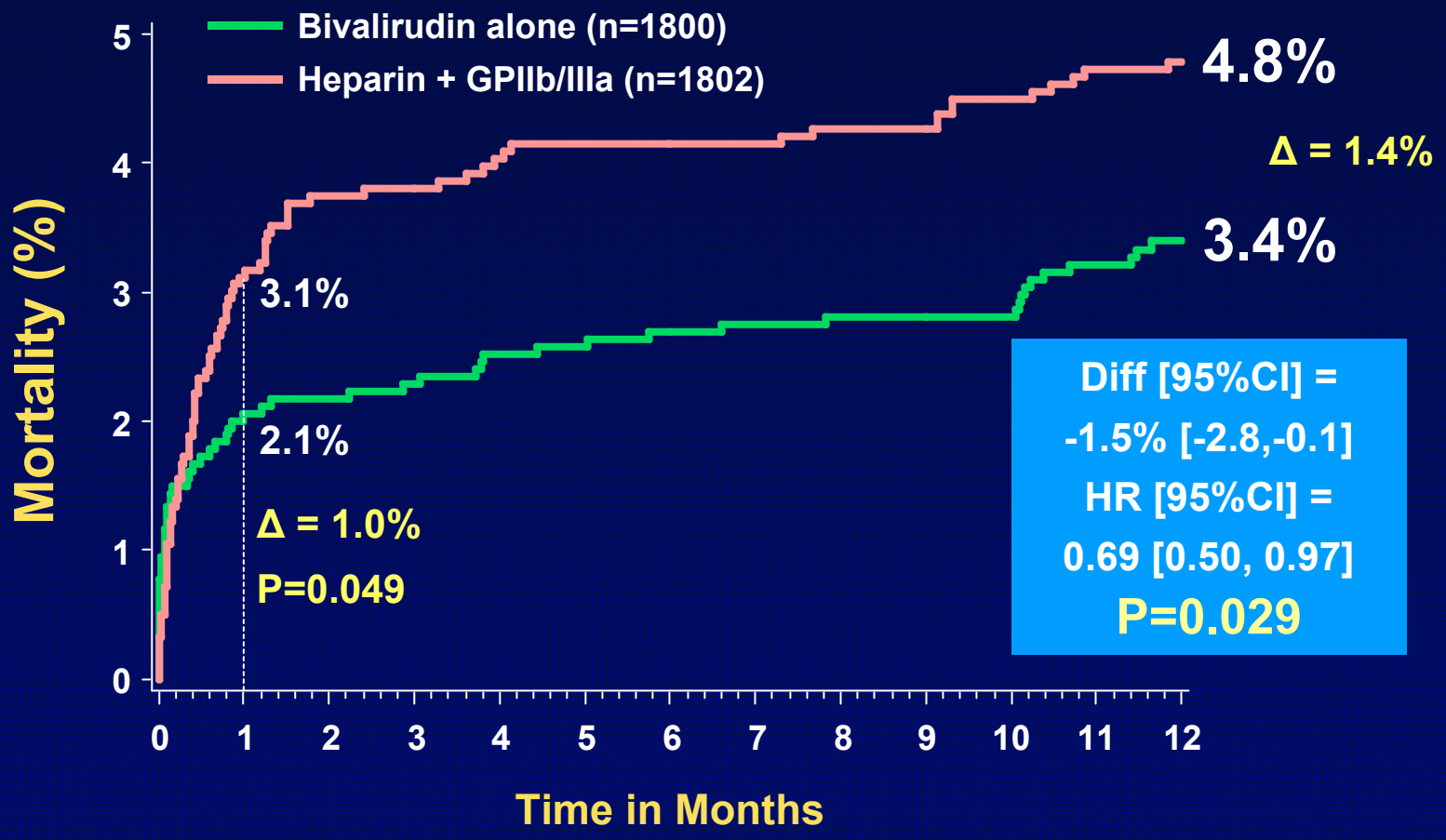
1-Year Major Adverse CV Events*



Number at risk					
Bivalirudin alone	1800	1627	1579	1544	1394
Heparin+GPIIb/IIIa	1802	1619	1573	1540	1380

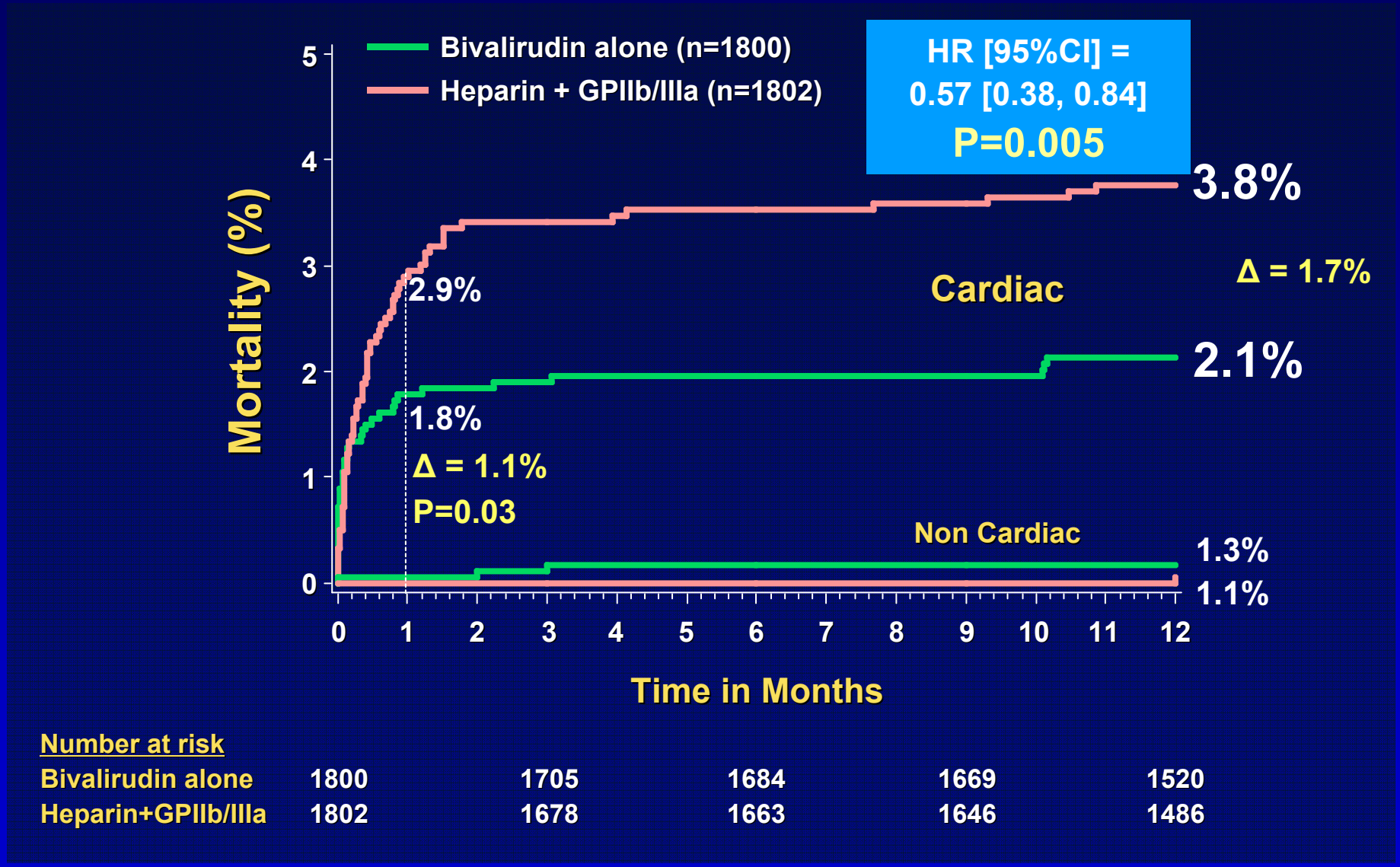
*MACE = All cause death, reinfarction, ischemic TVR or stroke

1-Year All-Cause Mortality



Number at risk					
Bivalirudin alone	1800	1705	1684	1669	1520
Heparin+GPIIb/IIIa	1802	1678	1663	1646	1486

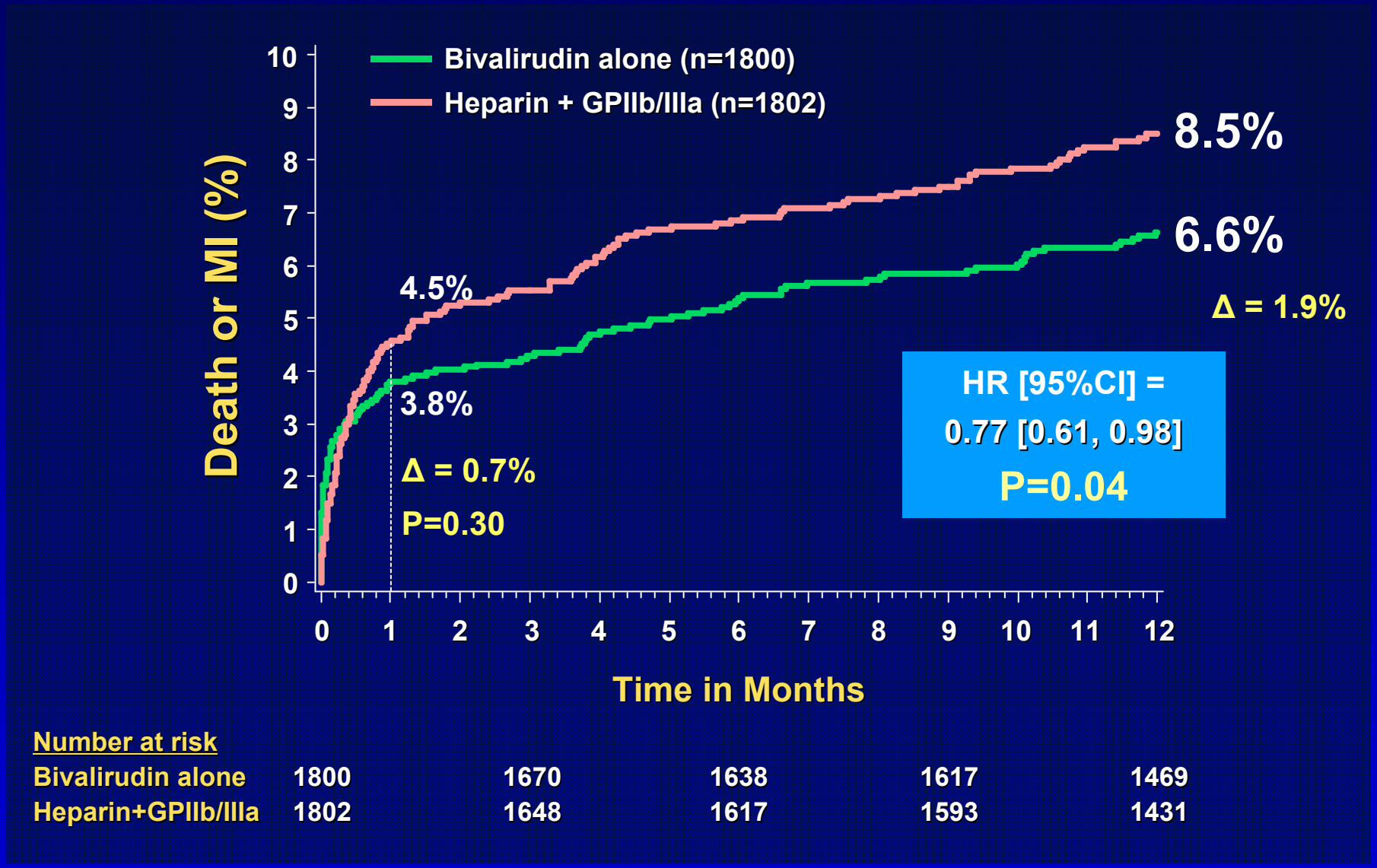
1-Year Mortality: Cardiac and Non Cardiac



Number at risk

Bivalirudin alone	1800	1705	1684	1669	1520
Heparin+GPIIb/IIIa	1802	1678	1663	1646	1486

1-Year Death or Reinfarction



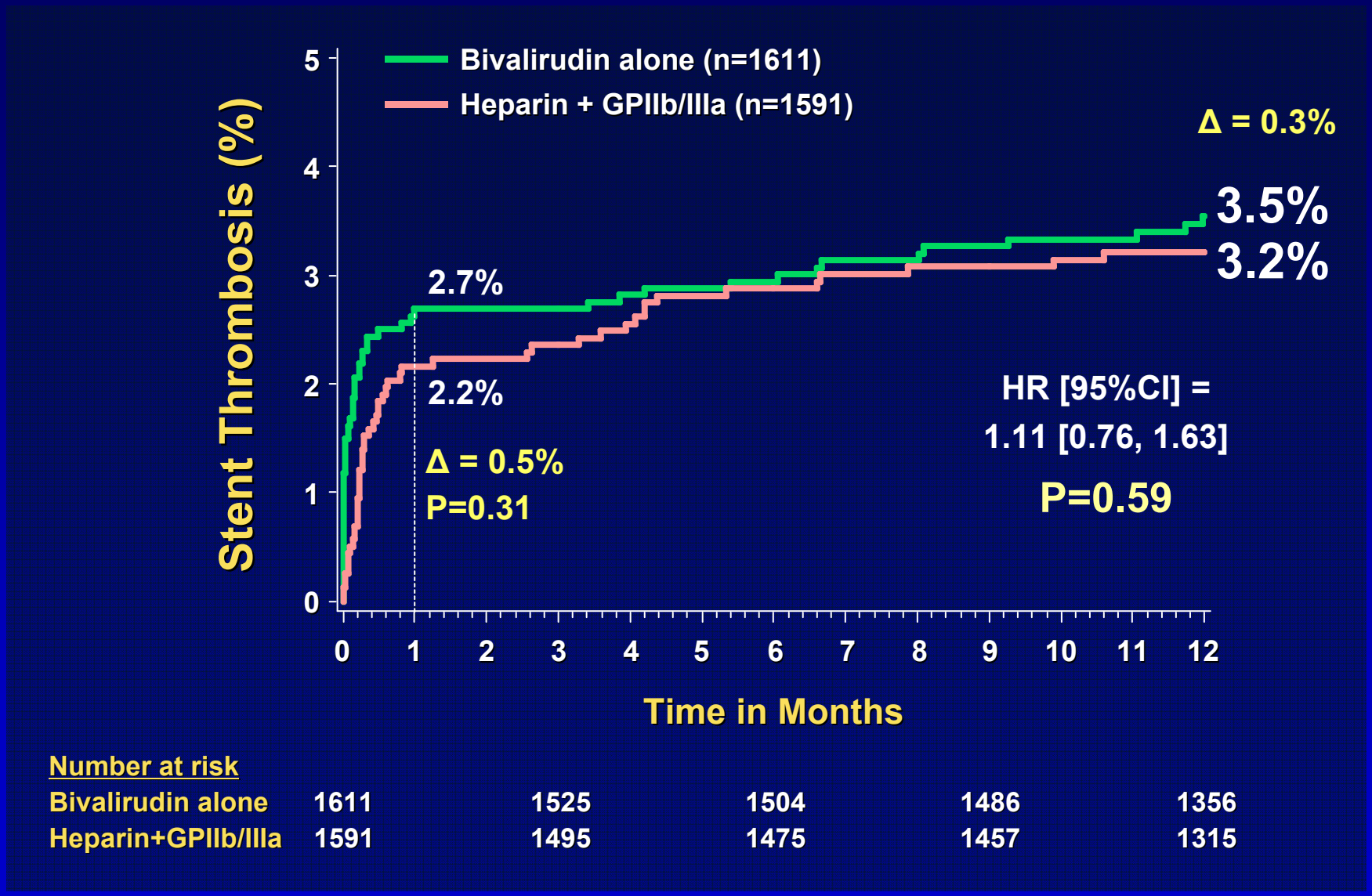
Number at risk					
Bivalirudin alone	1800	1670	1638	1617	1469
Heparin+GPIIb/IIIa	1802	1648	1617	1593	1431

Adverse Events Between 30 Days and 1-Year

	UFH + GPI (N=1802)	Bivalirudin (N=1800)	P Value
Death	1.8%	1.4%	0.31
- Cardiac	0.9%	0.4%	0.046
- Non cardiac	0.9%	1.0%	0.75
Reinfarction	2.8%	1.7%	0.04
Death or reinfarction	4.4%	3.0%	0.02
Ischemic TVR	4.3%	4.7%	0.57
Stroke	0.5%	0.4%	0.77
MACE	7.3%	6.8%	0.52
Major bleeding (non CABG)	0.7%	0.8%	0.71
NACE	7.8%	7.3%	0.52

*Kaplan-Meier estimates, landmark analysis, CEC adjudicated

1-Year Stent Thrombosis (ARC Definite/Probable)



Number at risk					
Bivalirudin alone	1611	1525	1504	1486	1356
Heparin+GPIIb/IIIa	1591	1495	1475	1457	1315

1-Year Stent Thrombosis* (N=3,202)

	UFH + GPI (N=1591)	Bivalirudin (N=1611)	P Value
ARC definite or probable, ≤24 hrs	0.3%	1.5%	0.0002
- definite, ≤24 hours	0.2%	1.4%	<0.0001
- probable, ≤24 hours	0.1%	0.1%	1.0
ARC definite or probable, >1 - ≤30d	1.9%	1.3%	0.14
- definite, >1 day - ≤30 days	1.3%	1.1%	0.60
- probable, >1 day - ≤30 days	0.6%	0.2%	0.049
ARC definite or probable, >30d – 1y	1.1%	0.9%	0.53
- definite, >30 days – 1-year	1.0%	0.9%	0.65
- probable, >30 days – 1-year	0.1%	0.1%	0.55
ARC definite or probable, ≤1-year	3.2%	3.5%	0.59
- definite, ≤1-year	2.4%	3.2%	0.15
- probable, ≤1-year	0.8%	0.3%	0.06

*All Kaplan-Meier estimates except ≤24 hours; all CEC adjudicated

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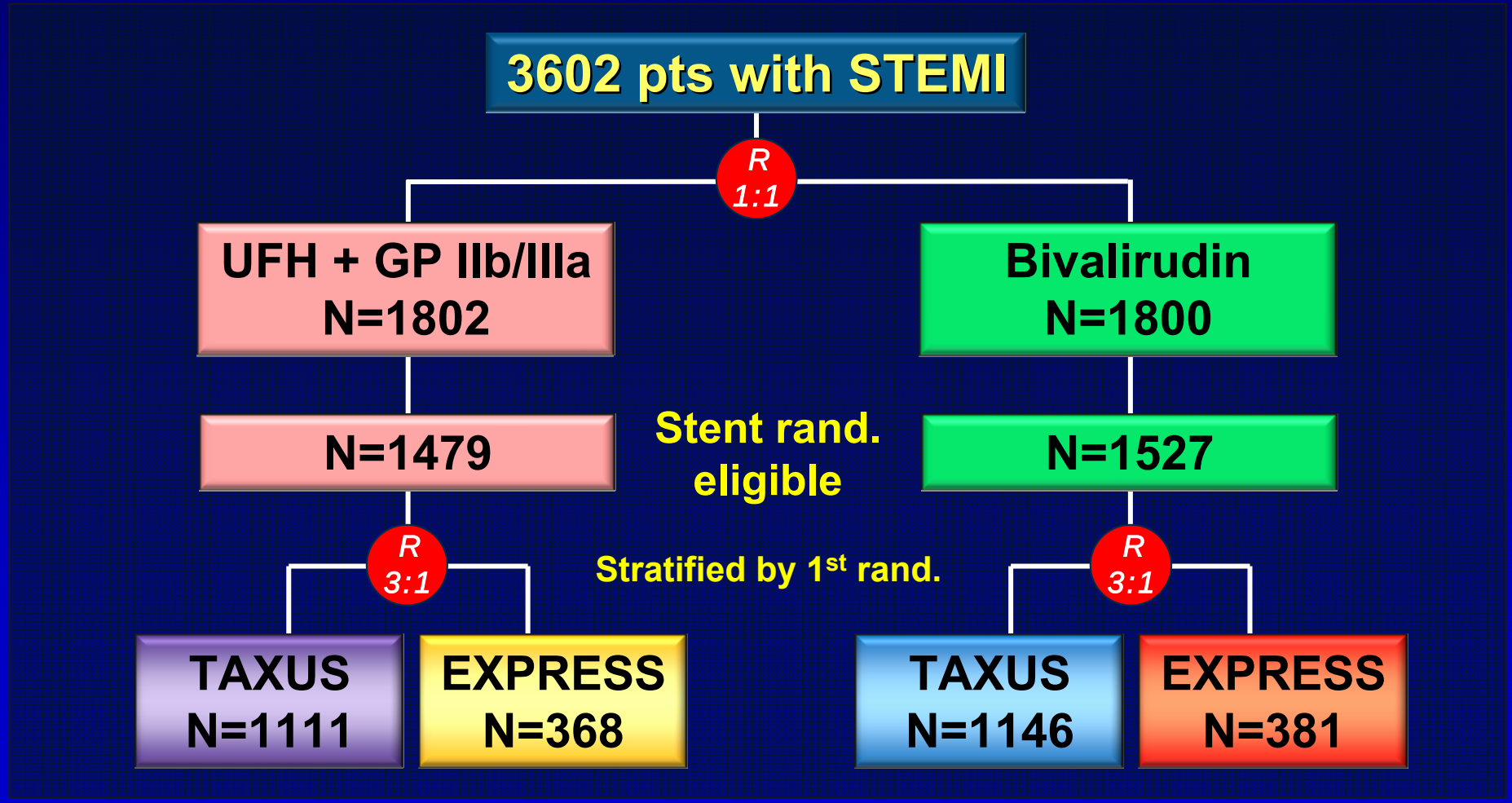


Interaction Between Drug and Stent Randomization

30 Day Pharmacology Endpoints (N=3006)

Kaplan-Meier estimates	UFH + GPI (N=1479)	Bivalirudin (N=1527)	HR [95%CI]	P_{int}
NACE, all*	11.3%	8.7%	0.76 [0.60,0.95]	-
- TAXUS subgroup	11.5%	9.1%	0.78 [0.60,1.01]	0.95
- EXPRESS subgroup	10.6%	7.4%	0.69 [0.42,1.11]	
Major bleeding, all**	8.4%	5.1%	0.59 [0.44,0.78]	-
- TAXUS subgroup	8.9%	5.4%	0.59 [0.43,0.81]	1.0
- EXPRESS subgroup	7.1%	4.2%	0.58 [0.31,1.09]	
MACE, all***	4.7%	4.9%	1.05 [0.75,1.45]	-
- TAXUS subgroup	4.6%	5.1%	1.11 [0.76,1.62]	0.89
- EXPRESS subgroup	4.9%	4.2%	0.86 [0.44,1.69]	

*MACE or major bleeding; **Protocol defined (non CABG); ***Death, reinfarction, stroke or ischemic TVR

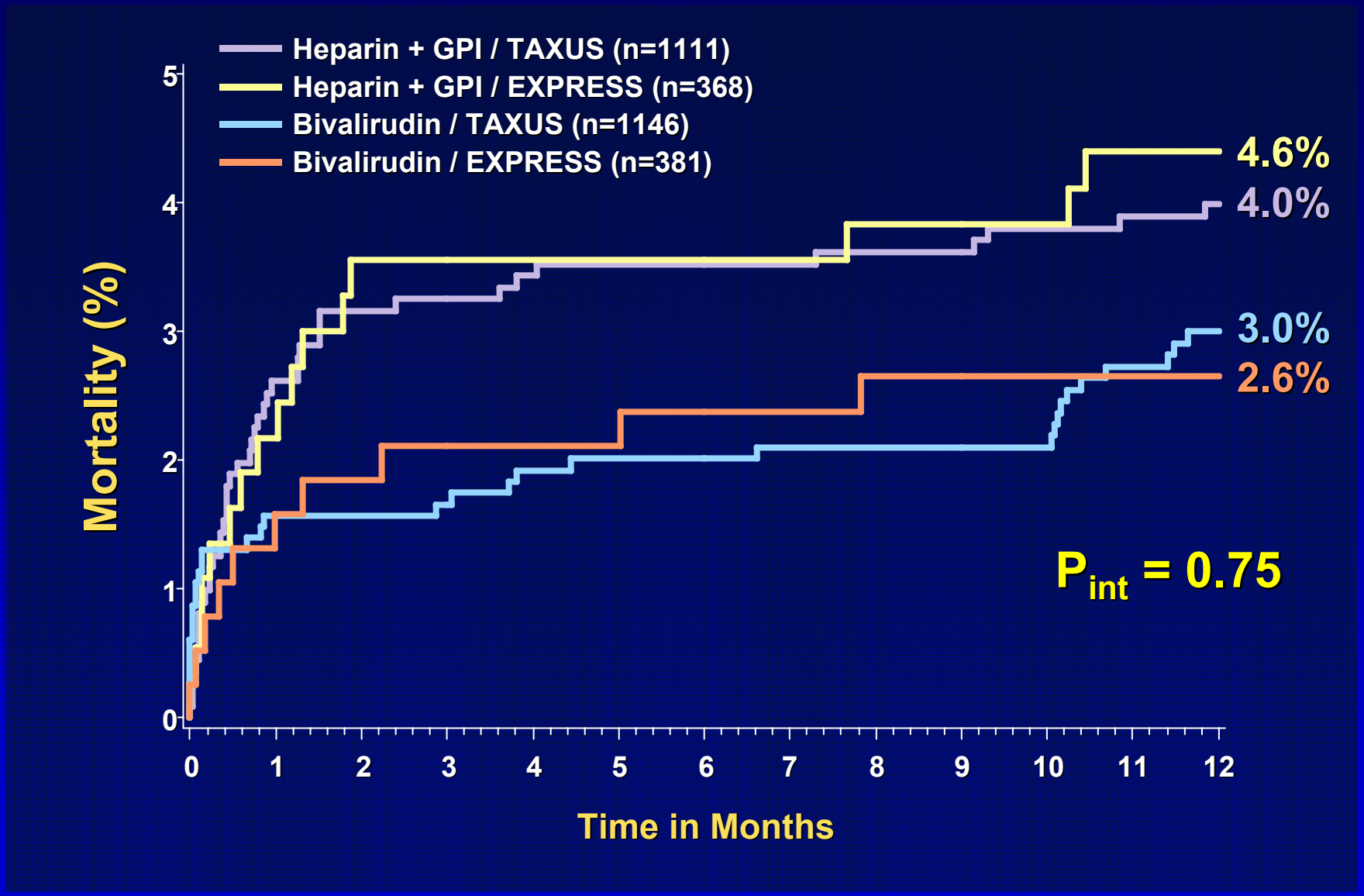
Interaction Between Drug and Stent Randomization

1-Year Stent Endpoints (N=3006)

Kaplan-Meier estimates	TAXUS (N=2257)	EXPRESS (N=749)	HR [95%CI]	P_{int}
Ischemic TLR, all	4.5%	7.5%	0.59 [0.43,0.83]	-
- UFH + GPI subgroup	3.3%	7.9%	0.42 [0.25,0.68]	0.17
- Bivalirudin subgroup	5.6%	7.1%	0.78 [0.50,1.24]	
Safety MACE, all*	8.1%	8.0%	1.02 [0.76, 1.36]	-
- UFH + GPI subgroup	8.2%	8.8%	0.92 [0.66,1.27]	0.89
- Bivalirudin subgroup	8.0%	7.2%	1.17 [0.83,1.64]	
Binary restenosis, all**	10.0%	22.9%	0.44 [0.33, 0.57]	-
- UFH + GPI subgroup	10.9%	19.2%	0.57 [0.38,0.84]	0.18
- Bivalirudin subgroup	9.2%	26.7%	0.34 [0.24,0.49]	

*Death, reinfarction, stroke or stent thrombosis
**1081 lesions in the TAXUS group, 332 in the EXPRESS group

1-Year Mortality (All-Cause)



Conclusions

- In this large scale, prospective, randomized trial of pts with STEMI undergoing a primary PCI management strategy, bivalirudin monotherapy compared to UFH plus the routine use of GP IIb/IIIa inhibitors resulted in:
  - A significant 16% reduction in the 1-year rate of composite net adverse clinical events
  - A significant 39% reduction in the 1-year rate of major bleeding

Conclusions

- In this large scale, prospective, randomized trial of pts with STEMI undergoing a primary PCI management strategy, bivalirudin monotherapy compared to UFH plus the routine use of GP IIb/IIIa inhibitors resulted in:
  - Significant 31% and 43% reductions in the 1-year rates of all-cause and cardiac mortality (absolute 1.4% and 1.7% reductions), with non significantly different rates of reinfarction, stent thrombosis, stroke and TVR at 1-year