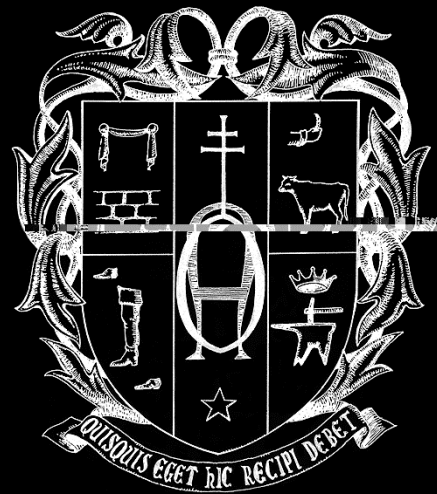


Santa Margherita Ligure
TIGULLIO CARDIOLOGIA 2012
16-17 Febbrajo 2012

Il trattamento dell'infarto miocardico acuto ad ST spraslivellato: dal territorio al laboratorio di emodinamica

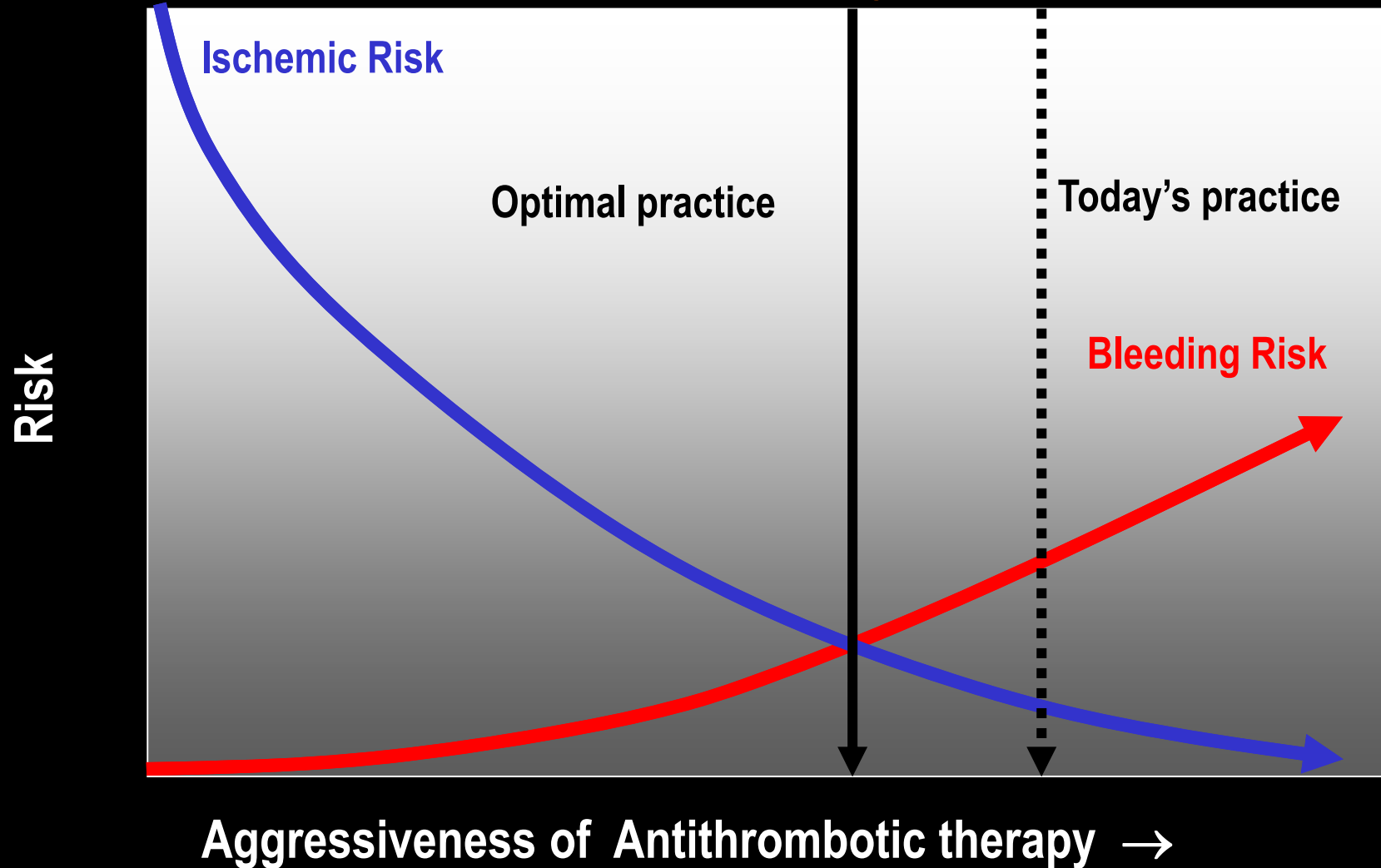
*Il punto sulla terapia antitrombotica
nelle sindromi coronariche acute*



Diego Ardissino
Parma

Ischemic vs Bleeding Risk in ACS

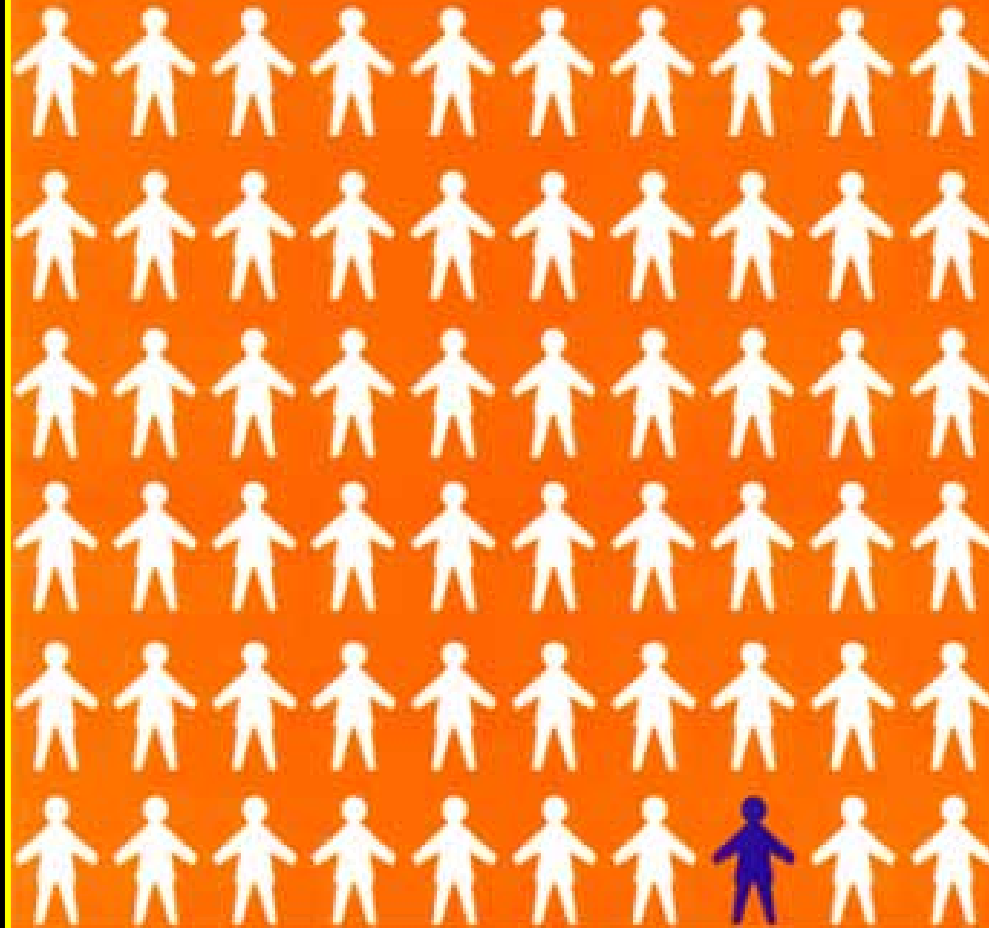
Antithrombotic therapy in ACS



nature
REVIEWS

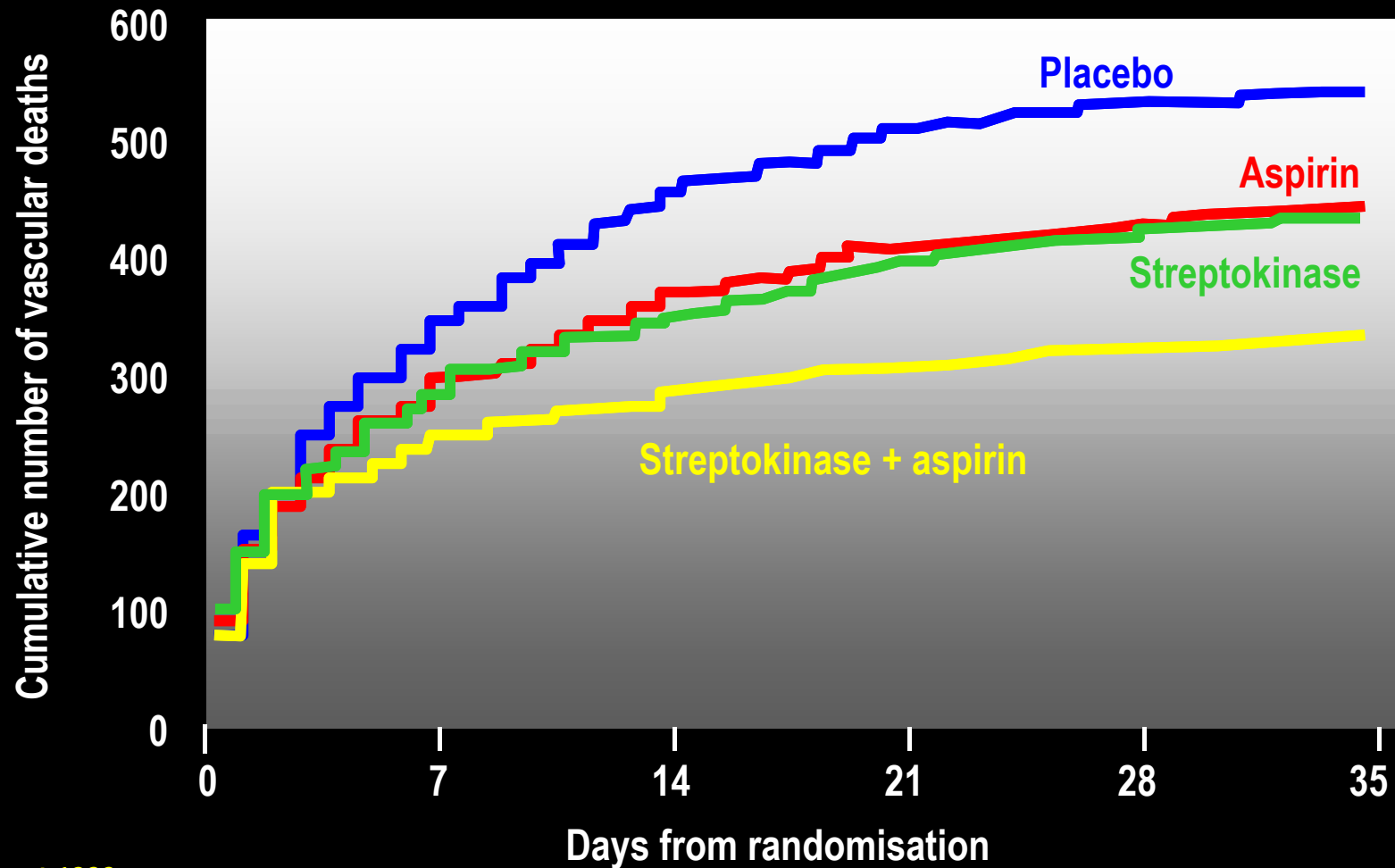
January 2013 Volume 2 No. 1
www.nature.com/reviews

DRUG DISCOVERY



Aspirin in Acute Myocardial Infarction

Cumulative vascular mortality in days 0 - 35



The Lancet 1988



Divisione di Cardiologia
Parma

ESC/ EACTS Guidelines on myocardial revascularization 2010

Antithrombotic treatment options in myocardial revascularization

Options for anticoagulation include UFH 60 IU/Kg iv bolus with GPIIb/IIIa inhibitor or UFH 100 IU/Kg iv bolus without GPIIb/IIIa inhibitor, (I C) or bivalirudin 0.75 mg/Kg bolus followed by 1.75 mg/kg/h (I B). Antithrombins can be stopped after PCI for STEMI.

EUROPEAN SOCIETY OF CARDIOLOGY GUIDELINES
MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

ANTITHROMBOTIC THERAPY IN PRIMARY PCI

Unfractionated heparin is standard anticoagulant therapy during PCI.

- i.v. bolus: 100 U/Kg (60 U/Kg if GP IIb/IIIa antagonists are used)
- target ACT during procedure: 250-350 seconds (200-250 seconds if GP IIb/IIIa antagonists are used)

CLASS I

EVIDENCE C

EUROPEAN SOCIETY OF CARDIOLOGY GUIDELINES
MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

ANTITHROMBOTIC THERAPY IN PRIMARY PCI

Abiciximab can be administered in primary PCI.

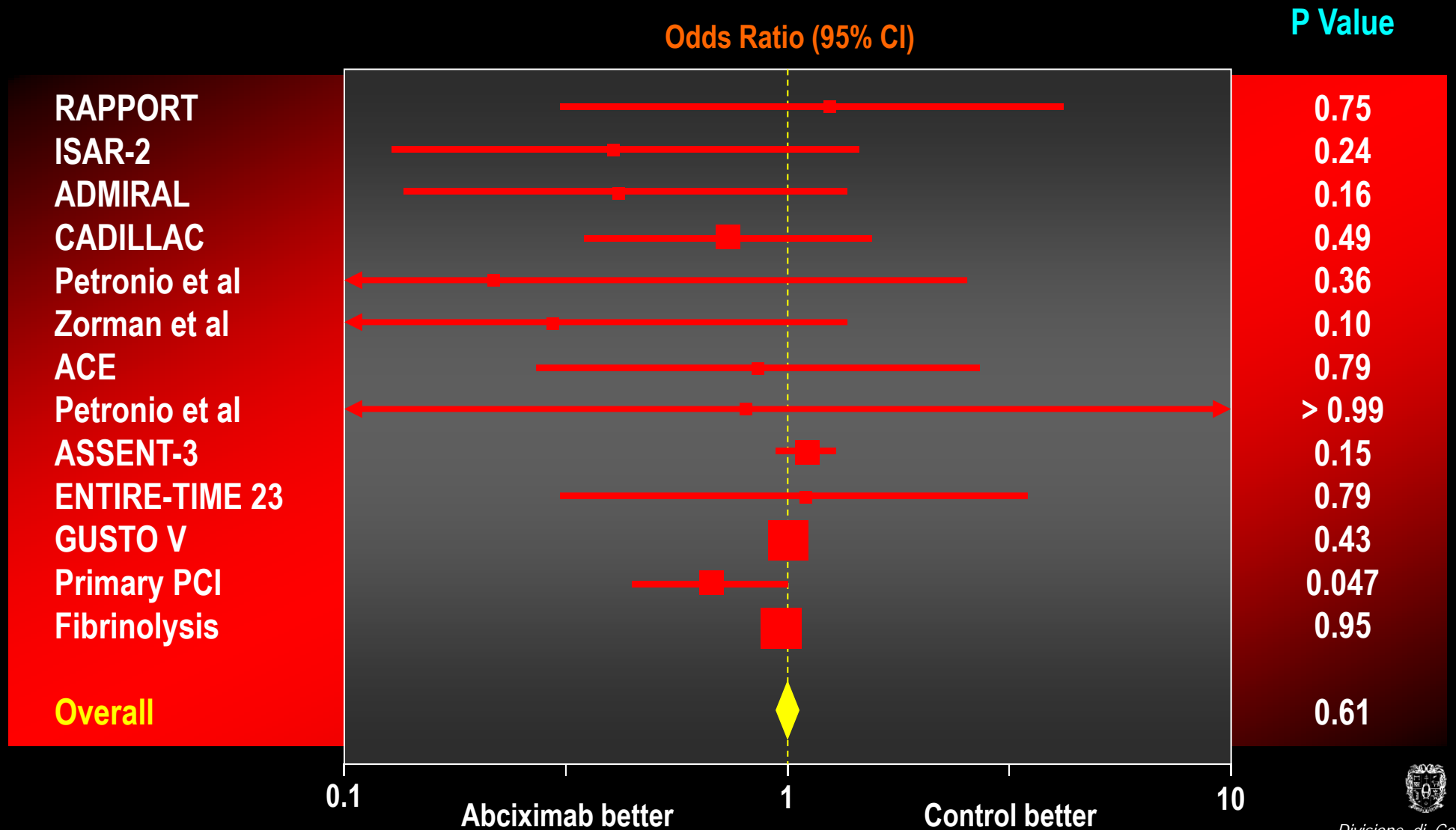
- i.v. bolus: 0.25 mg/kg
- Infusion: 0.125 mcg/Kg/min (maximum 10 mcg/min for 12 hours)

CLASS IIa

EVIDENCE A

Abciximab as Adjunctive Therapy to Reperfusion in STEMI

30-day mortality



Abciximab as Adjunctive Therapy to Reperfusion in STEMI

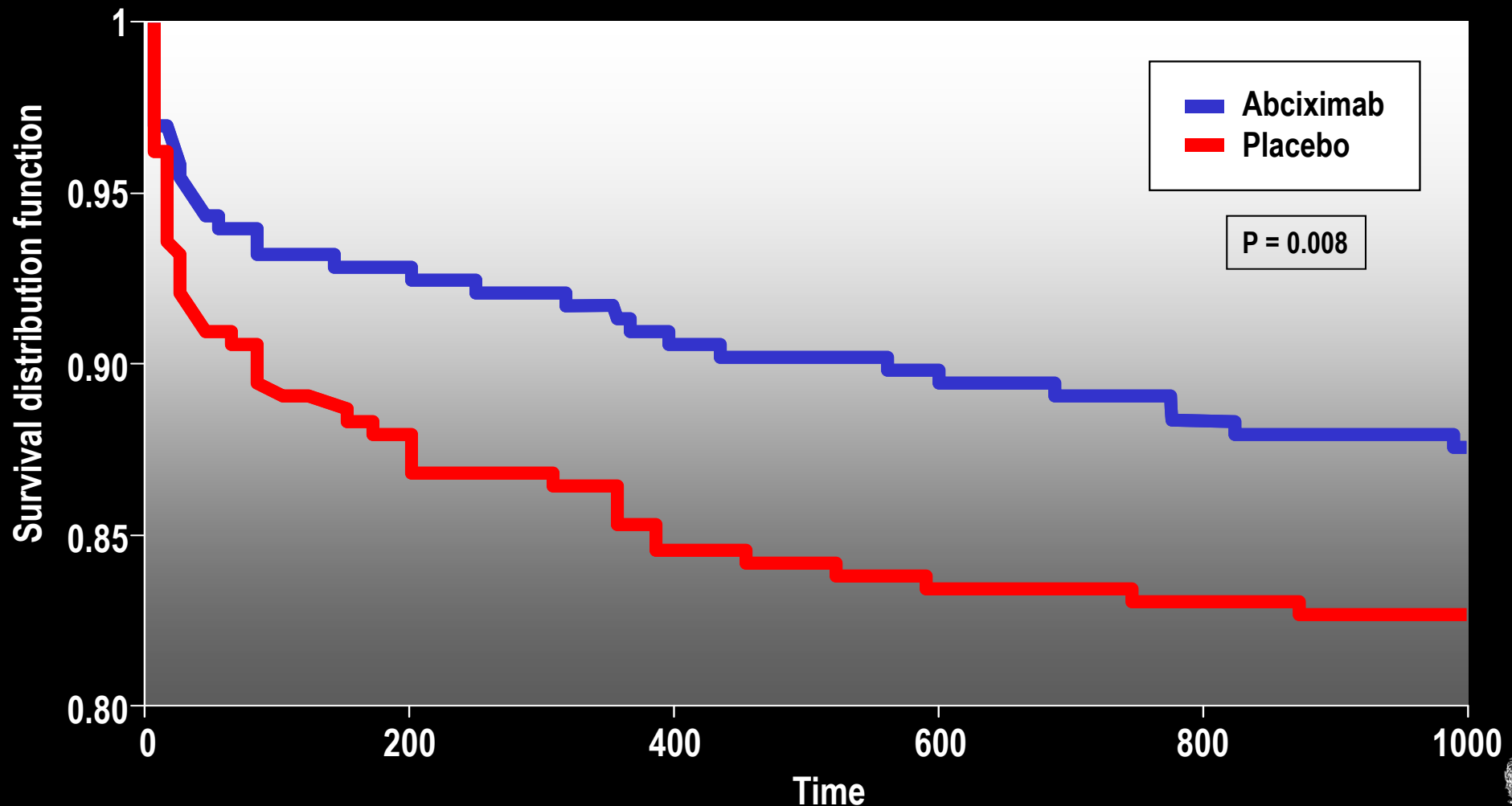
Long-term (6 and 12 month) mortality



Abciximab vs Placebo in Primary PCI

Death or re-infarction over 3 years of follow-up

Trials: ACE, ADMIRAL and ISAR



ESC/ EACTS Guidelines on myocardial revascularization 2010
Antithrombotic treatment options in myocardial revascularization

UPSTREAM GP IIb/IIIa INHIBITORS

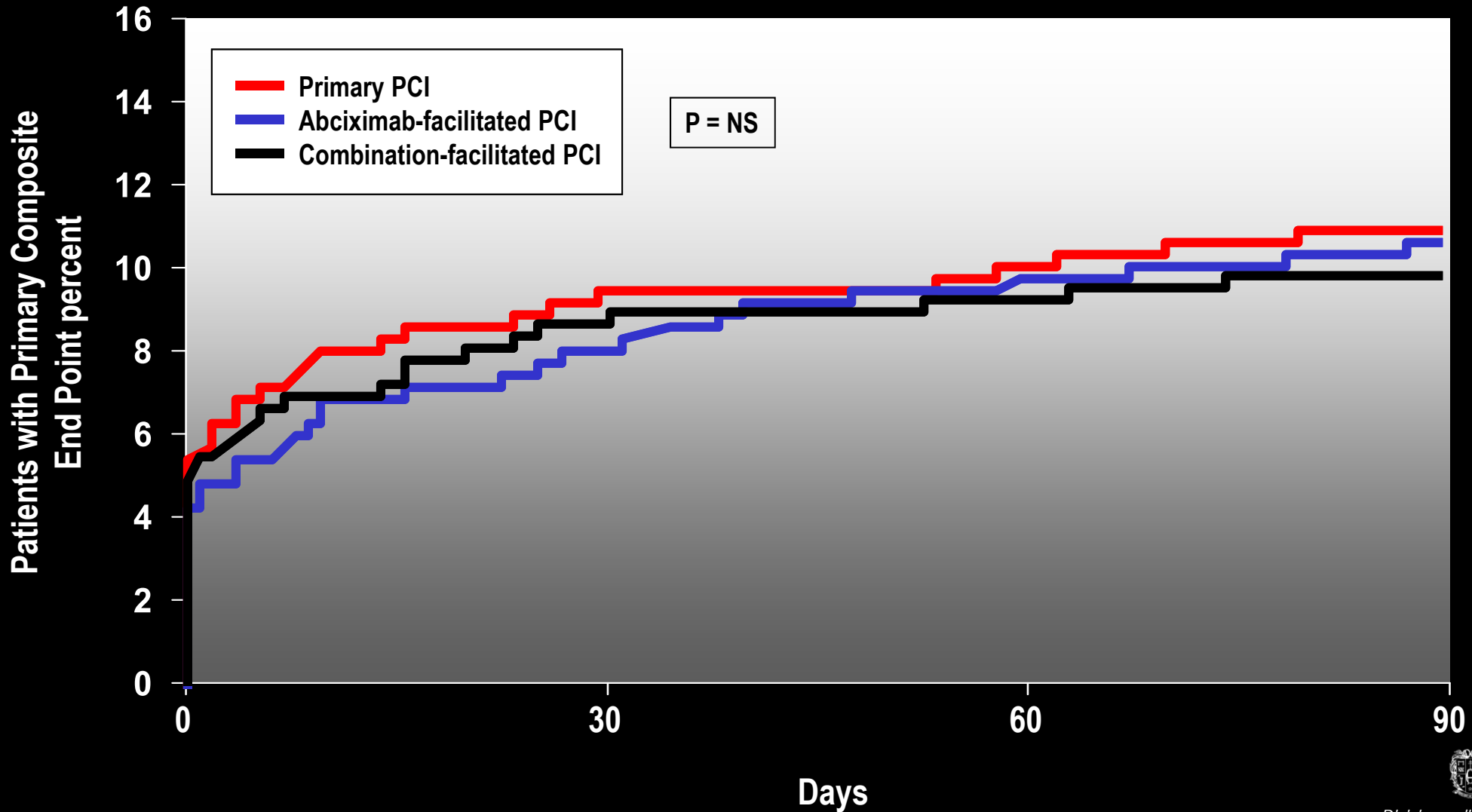
...the controversial literature data, the negative outcome of the only prospective RCT and the beneficial effects of faster acting and more efficacious ADP receptor blockers in primary PCI do not support pre-hospital or pre-catheterization use of GPIIb/IIIa inhibitors.

CLASS III

EVIDENCE B

Facilitated PCI in Patients with STEMI

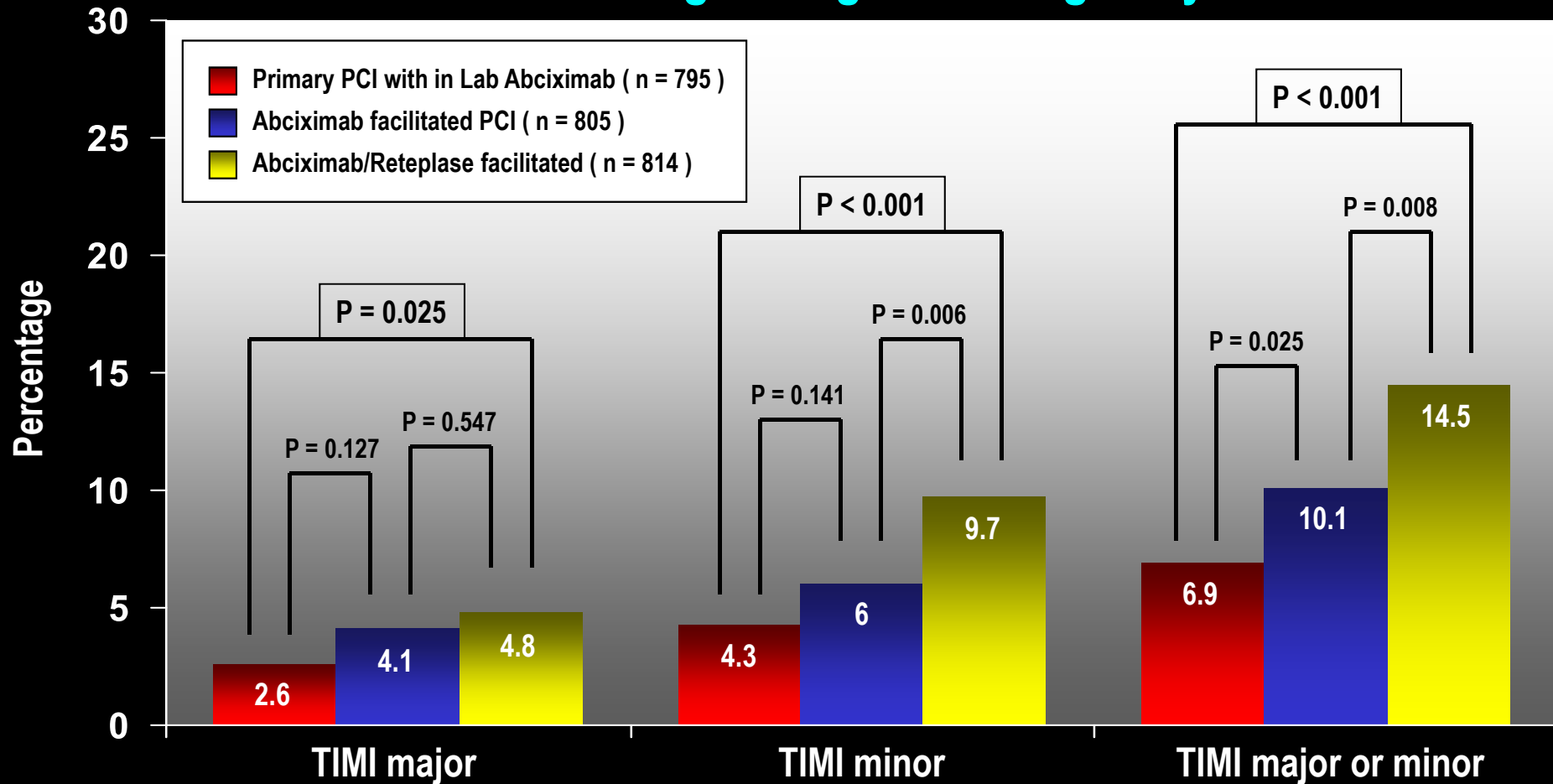
The FINESSE trial



Facilitated PCI in Patients with STEMI

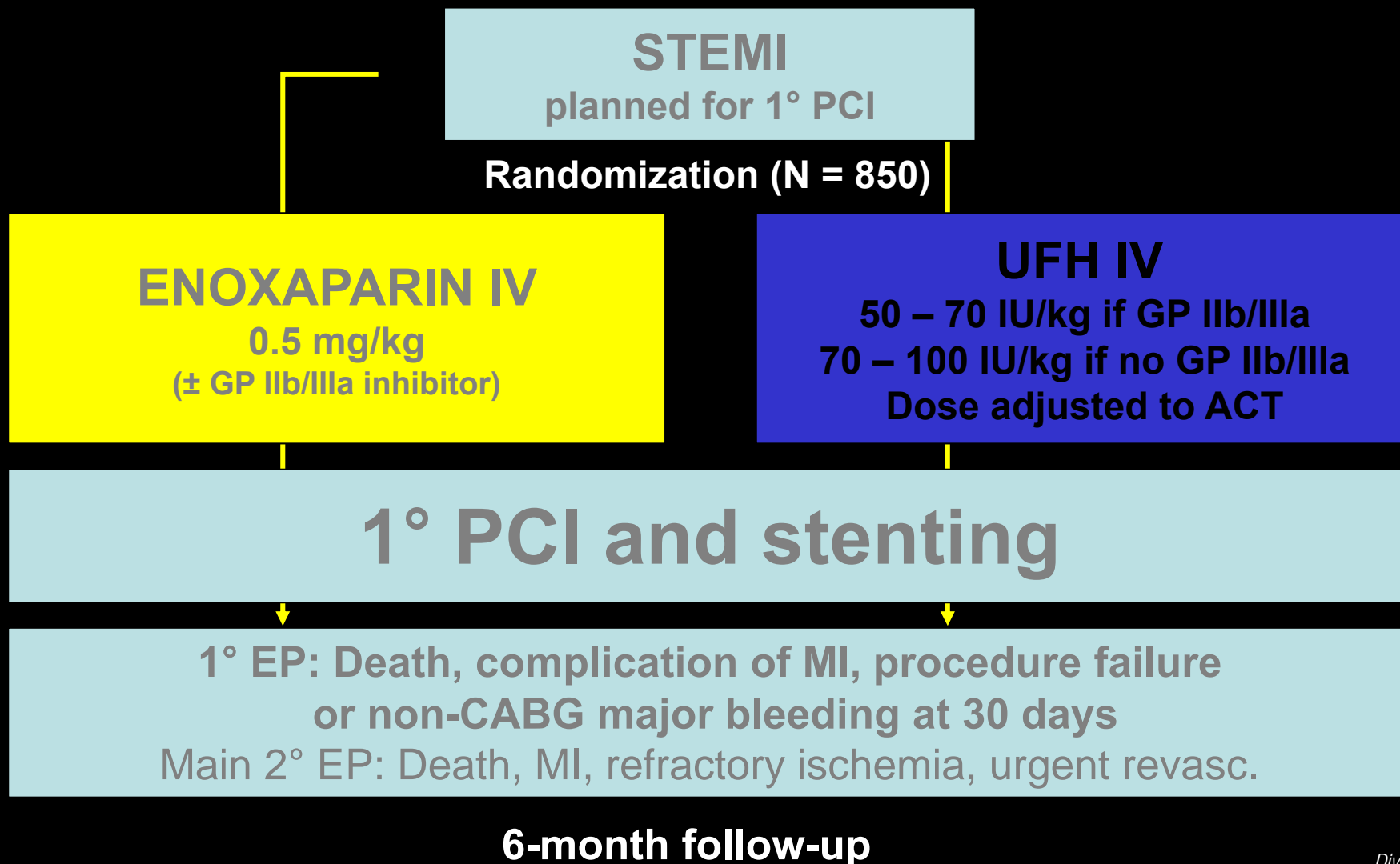
The FINESSE trial

TIMI Bleeding through Discharge/Day 7



Enoxaparin vs UFH in primary PCI

ATOLL Study Design



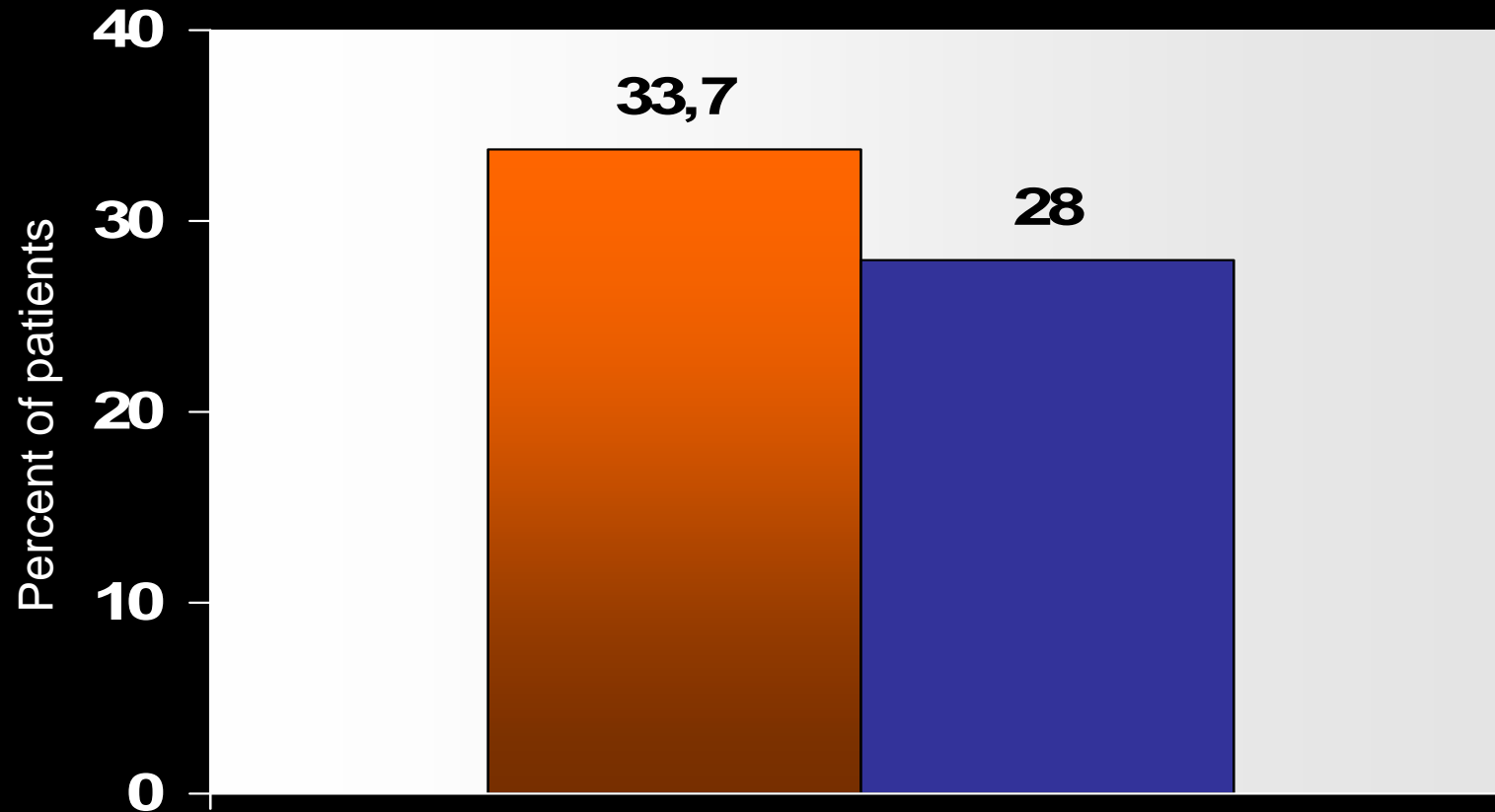
Enoxaparin vs UFH in primary PCI

ATOLL trial Primary endpoint

Death, complication of MI, procedure failure or maior bleeding

RRR=17%

P=0.07



ESC/ EACTS Guidelines on myocardial revascularization 2010
Antithrombotic treatment options in myocardial revascularization

ANTICOAGULATION

....a recent study suggested bivalirudin monotherapy as an alternative to UFH plus a GPIIb/IIIa inhibitor.

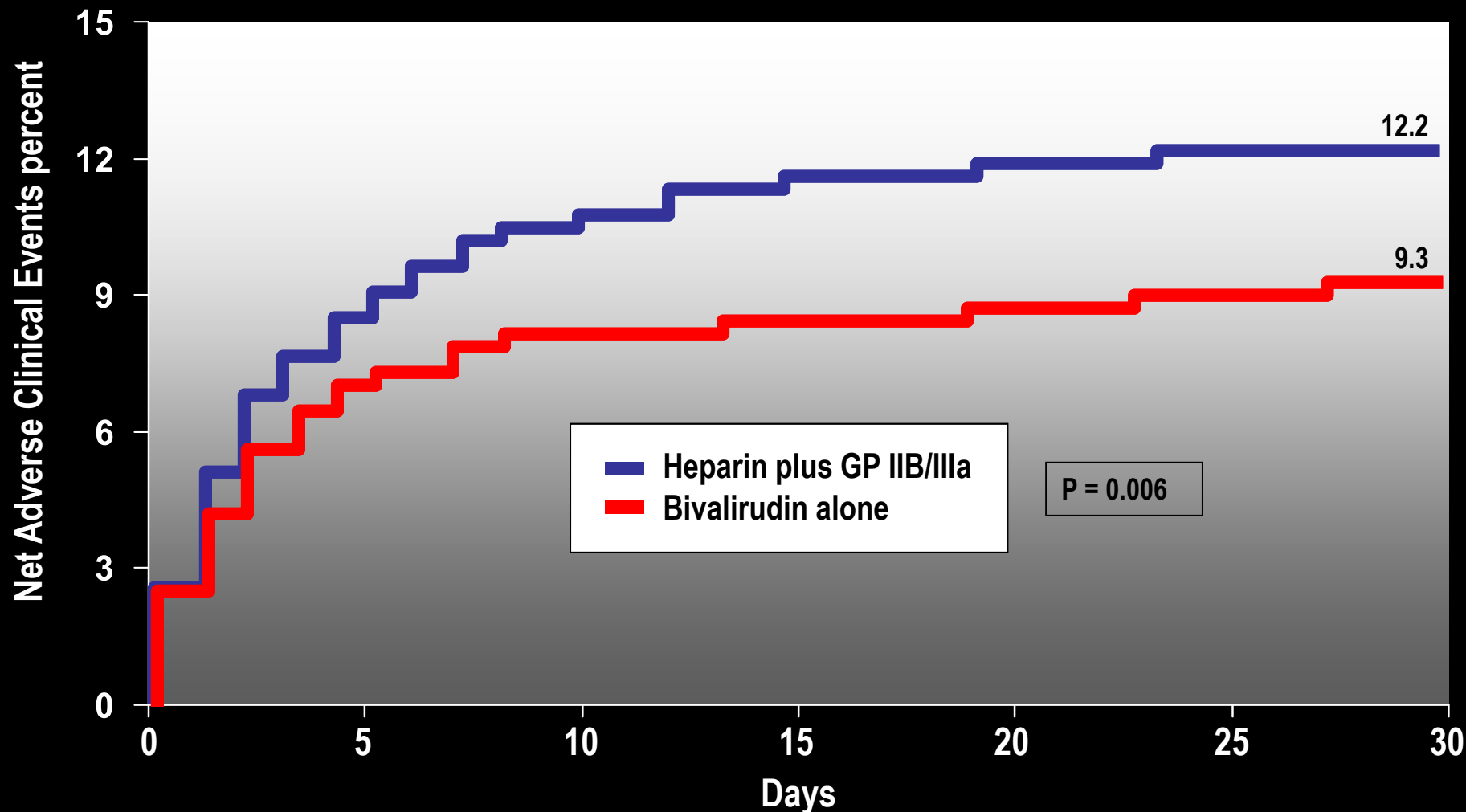
CLASS I

EVIDENCE B

Bivalirudin During Primary PCI in STEMI

The HORIZONS-AMI trial

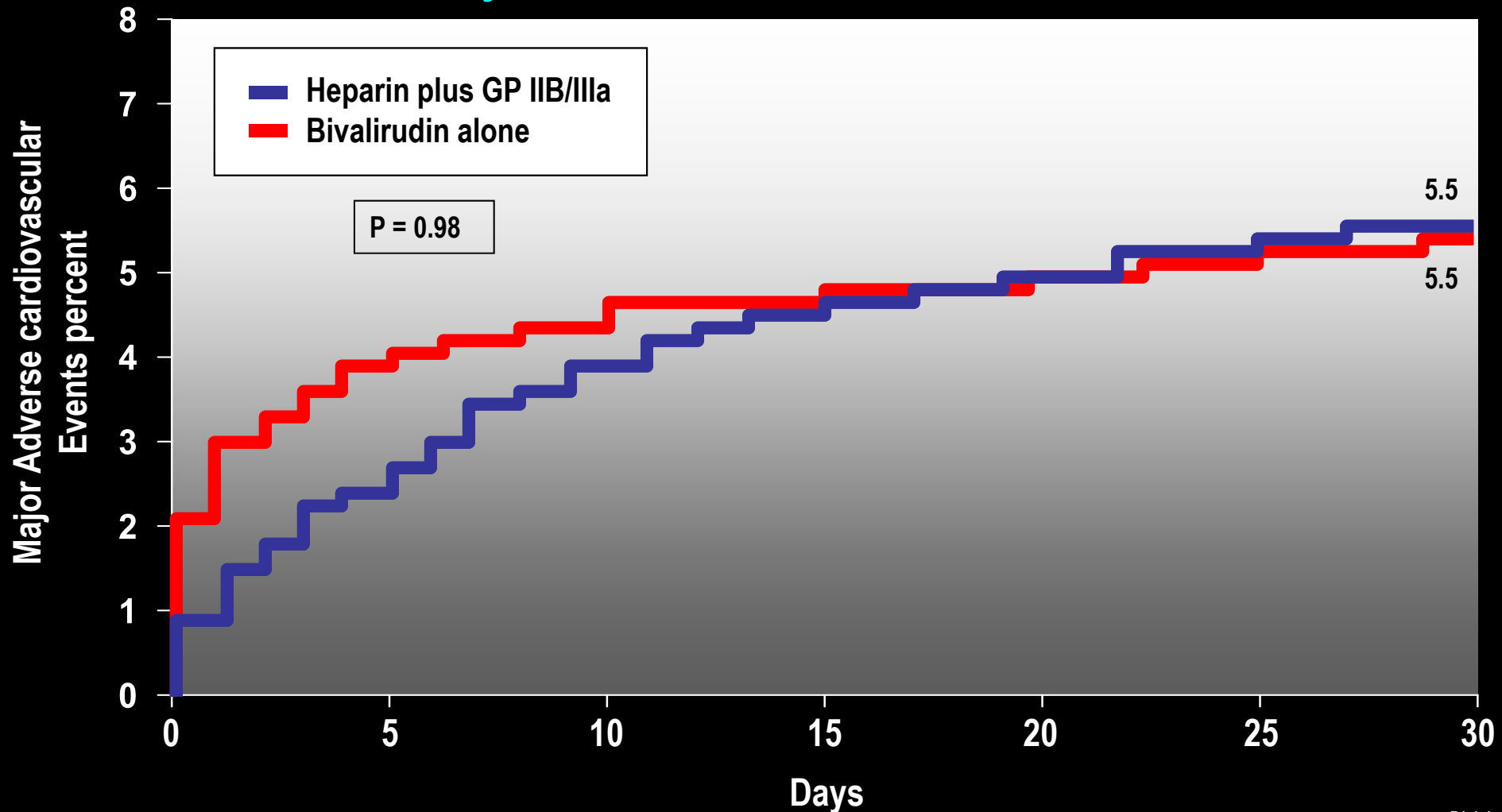
Net adverse clinical events



Bivalirudin During Primary PCI in STEMI

The HORIZONS-AMI trial

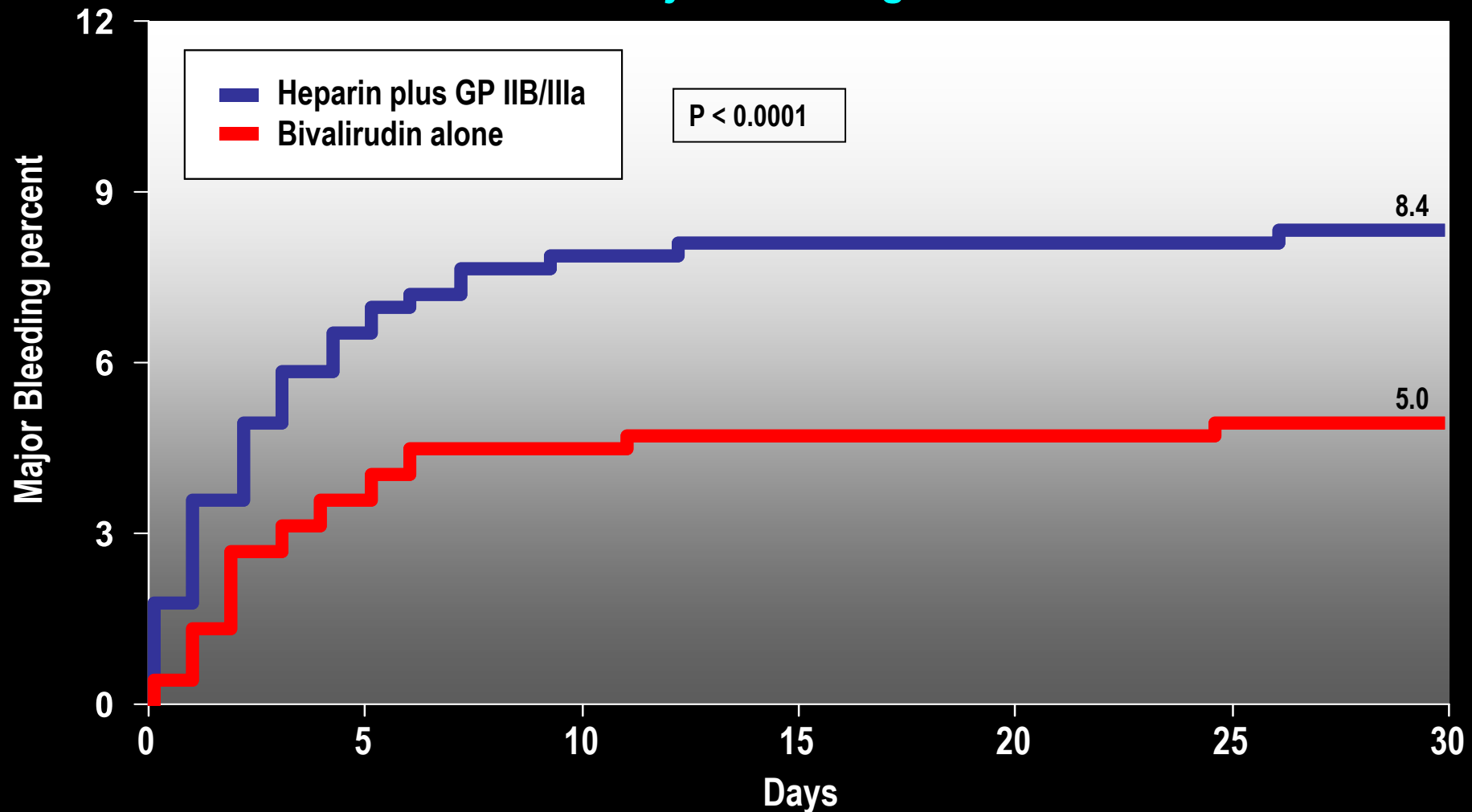
Major adverse cardiovascular events



Bivalirudin During Primary PCI in STEMI

The HORIZONS-AMI trial

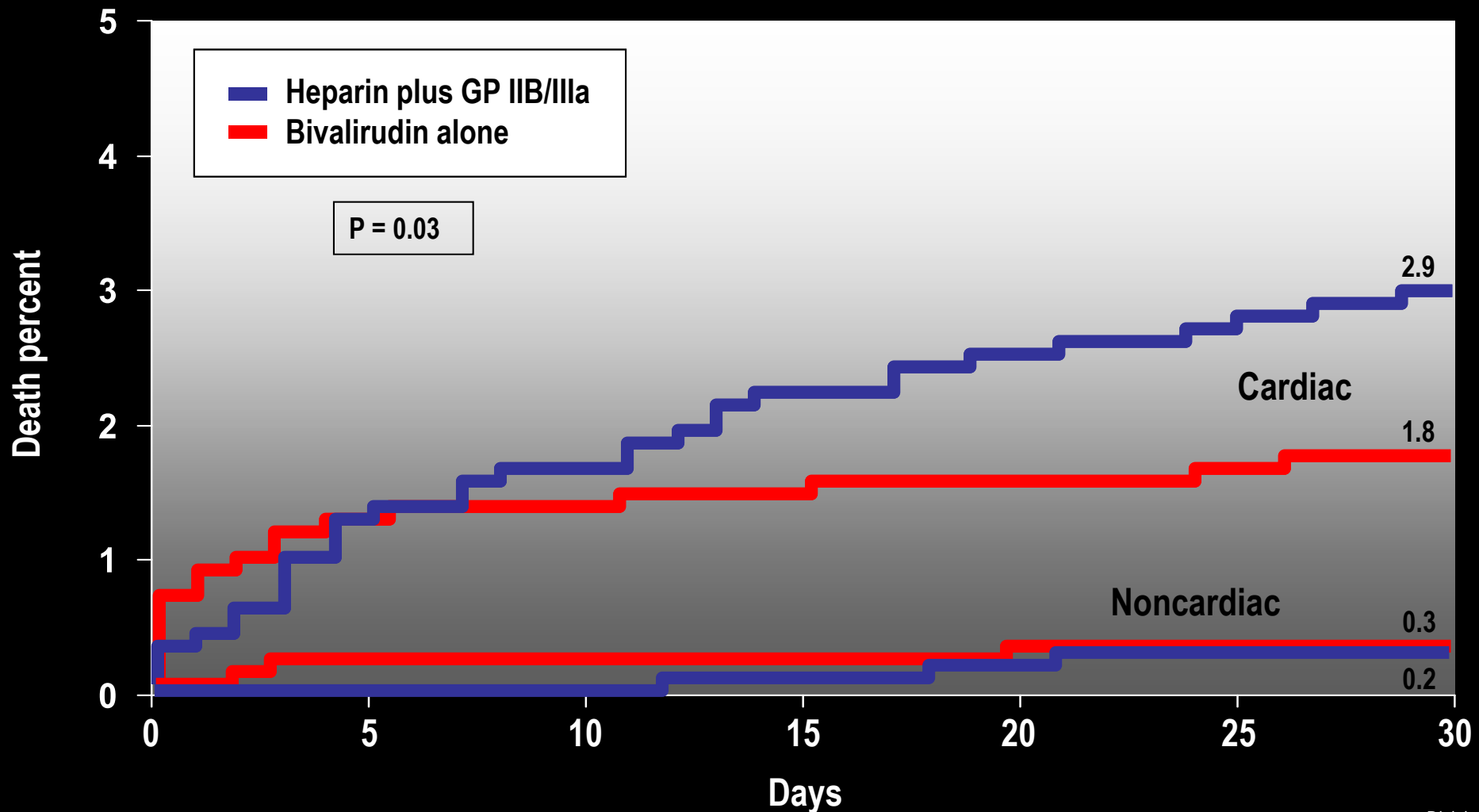
Major bleeding



Bivalirudin During Primary PCI in STEMI

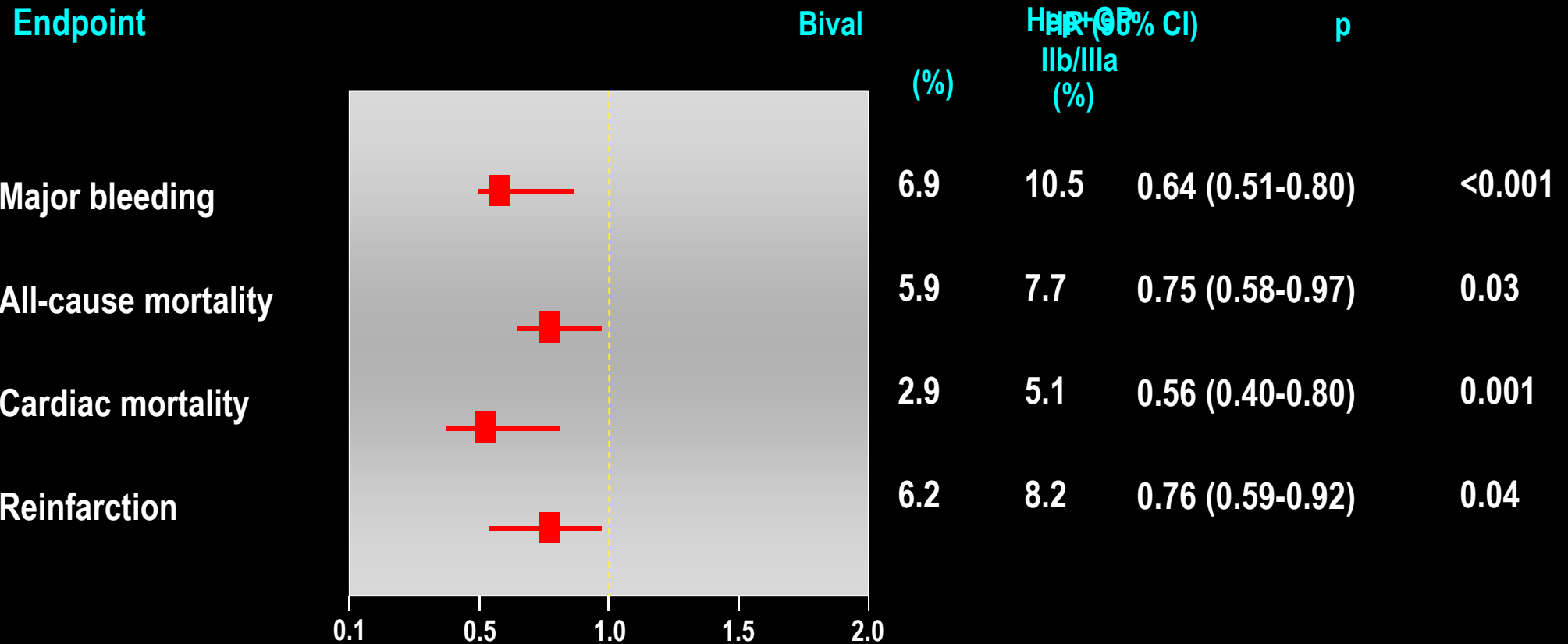
The HORIZONS-AMI trial

Death from cardiac and non cardiac causes



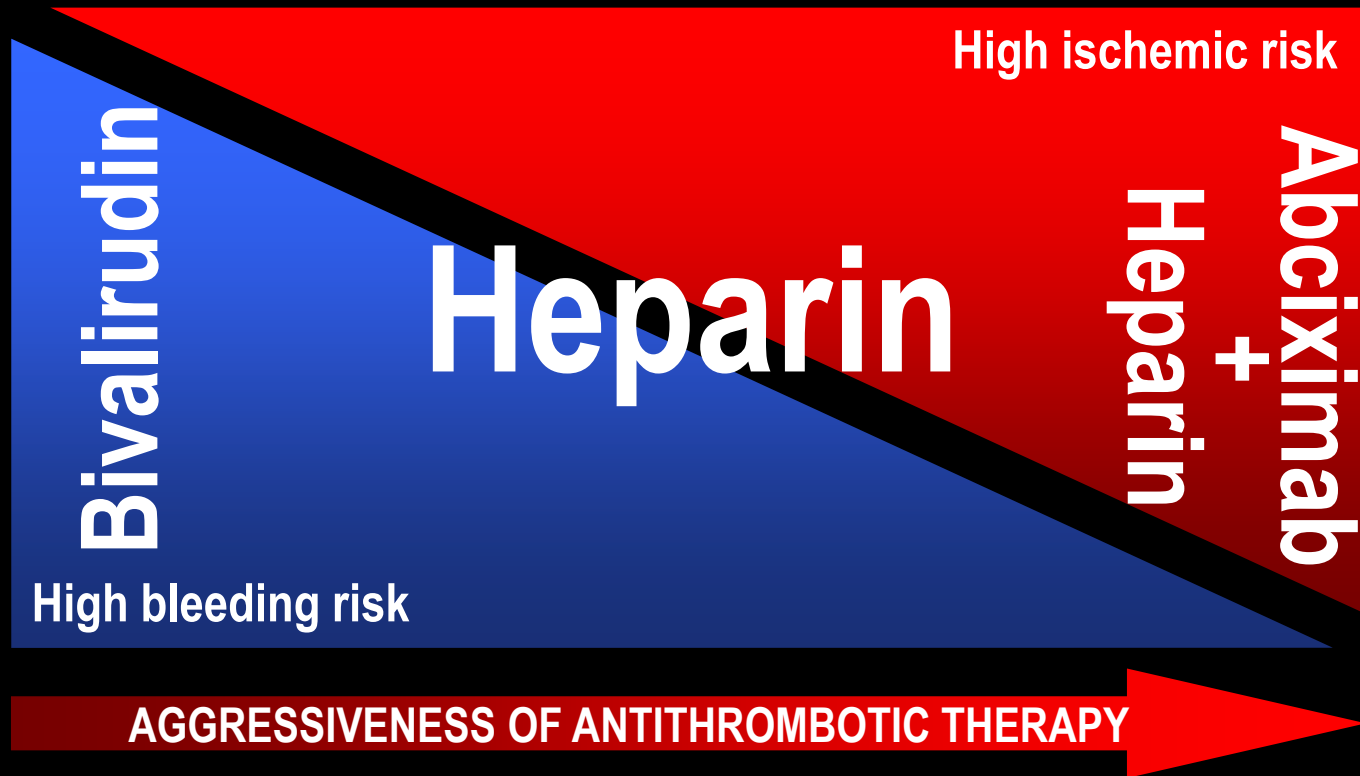
Bivalirudin During Primary PCI in STEMI

The HORIZONS-AMI trial 3-years follow up



ANTITHROMBOTIC THERAPY IN STEMI

Abciximab vs bivalirudin



ESC/ EACTS Guidelines on myocardial revascularization 2010
Antithrombotic treatment options in myocardial revascularization

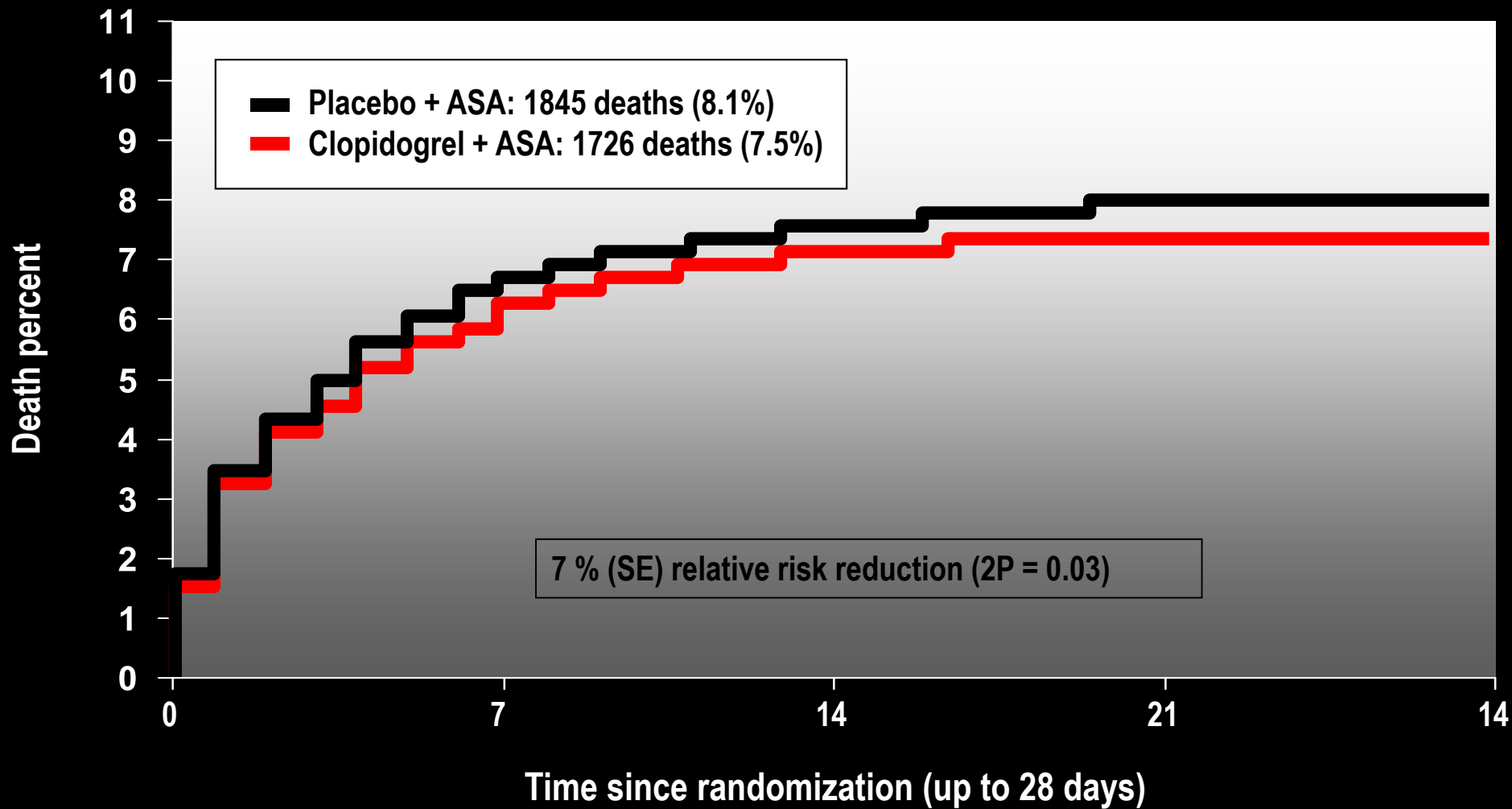
STEMI ANTITHROMBOTIC THERAPY

Dual antiplatelet therapy consists of aspirin 150-300mg per os or 250-500 mg bolus iv followed by 75-100 mg daily, and prasugrel 60 mg loading dose, followed by 10 mg daily, or ticagrelor 180 mg loading dose, followed by 90 mg twice daily, depending on drug availability.

Clopidogrel 600 mg loading dose, followed by 75 mg daily should be used primarily if the more effective ADP receptor blockers are contraindicated or unavailable.

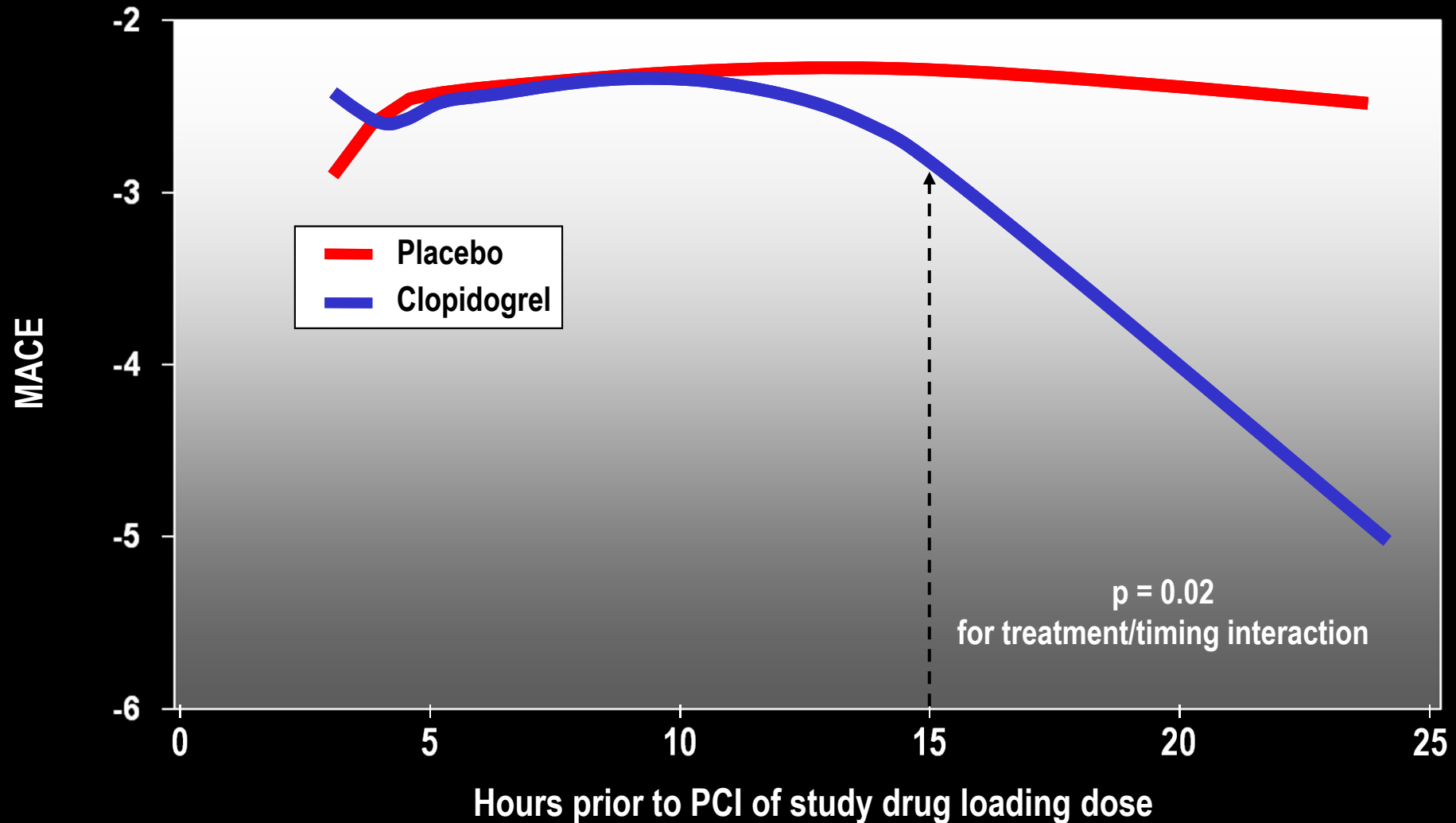
COMMIT / CCS-2

In-hospital death



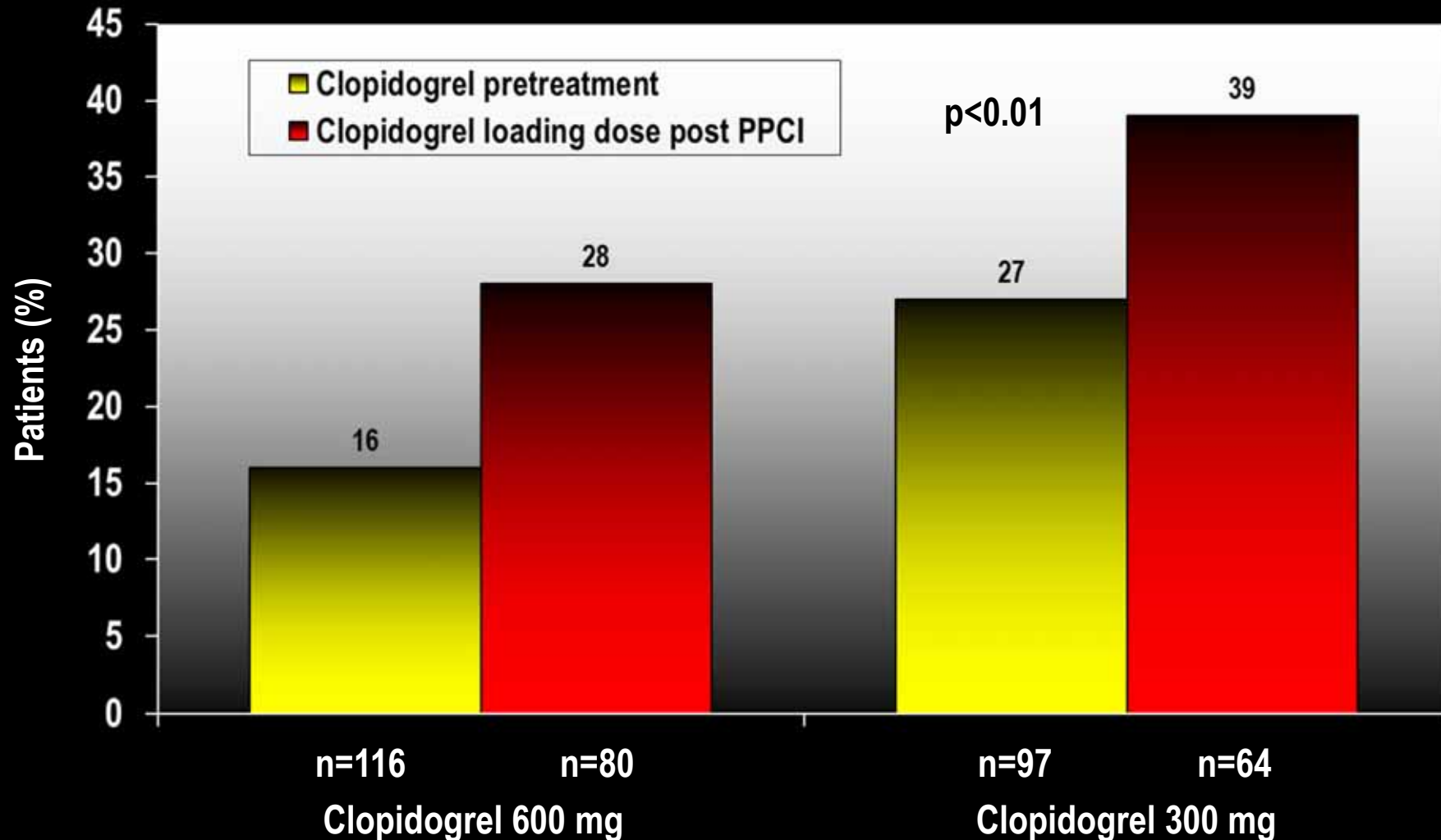
Prevention of Myocardial Infarction During PCI

Effect of Clopidogrel 300 mg Loading Dose



Impact of pre-treatment with clopidogrel on outcome in STEMI

Primary composite endpoint at 30 days (death, recurrent ACS, stent thrombosis, CHF)



ESC/ EACTS Guidelines on myocardial revascularization 2010

Antithrombotic treatment options in myocardial revascularization

Prasugrel is superior to clopidogrel in reducing combined ischaemic endpoints and stent thrombosis in STEMI patients without increasing the risk of severe bleeding.

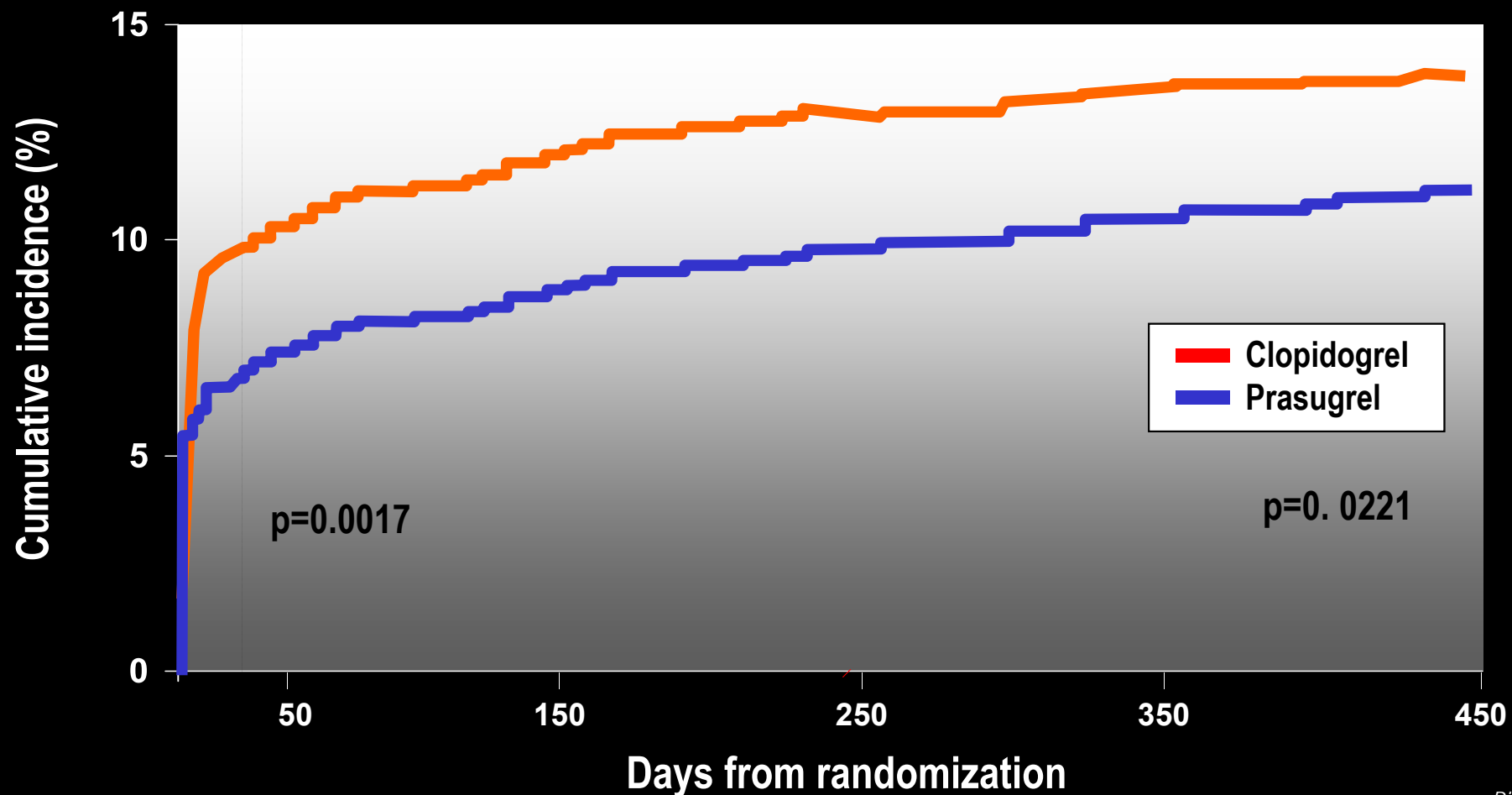
CLASS I

EVIDENCE B

Prasugrel vs clopidogrel in primary PCI

TRITON TIMI-38

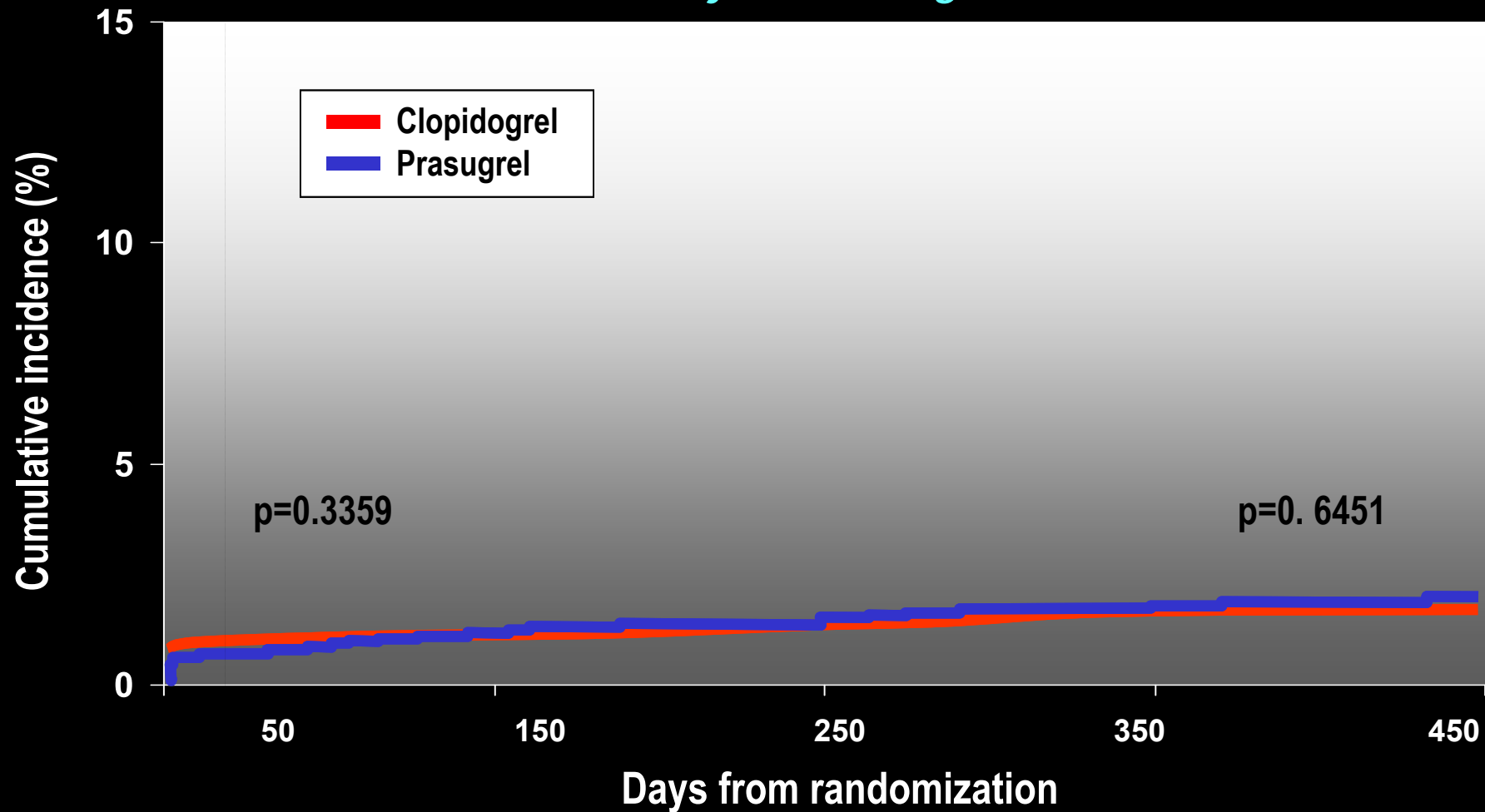
Primary endpoint: Cardiovascular death, non-fatal MI, non-fatal stroke



Prasugrel vs clopidogrel in primary PCI

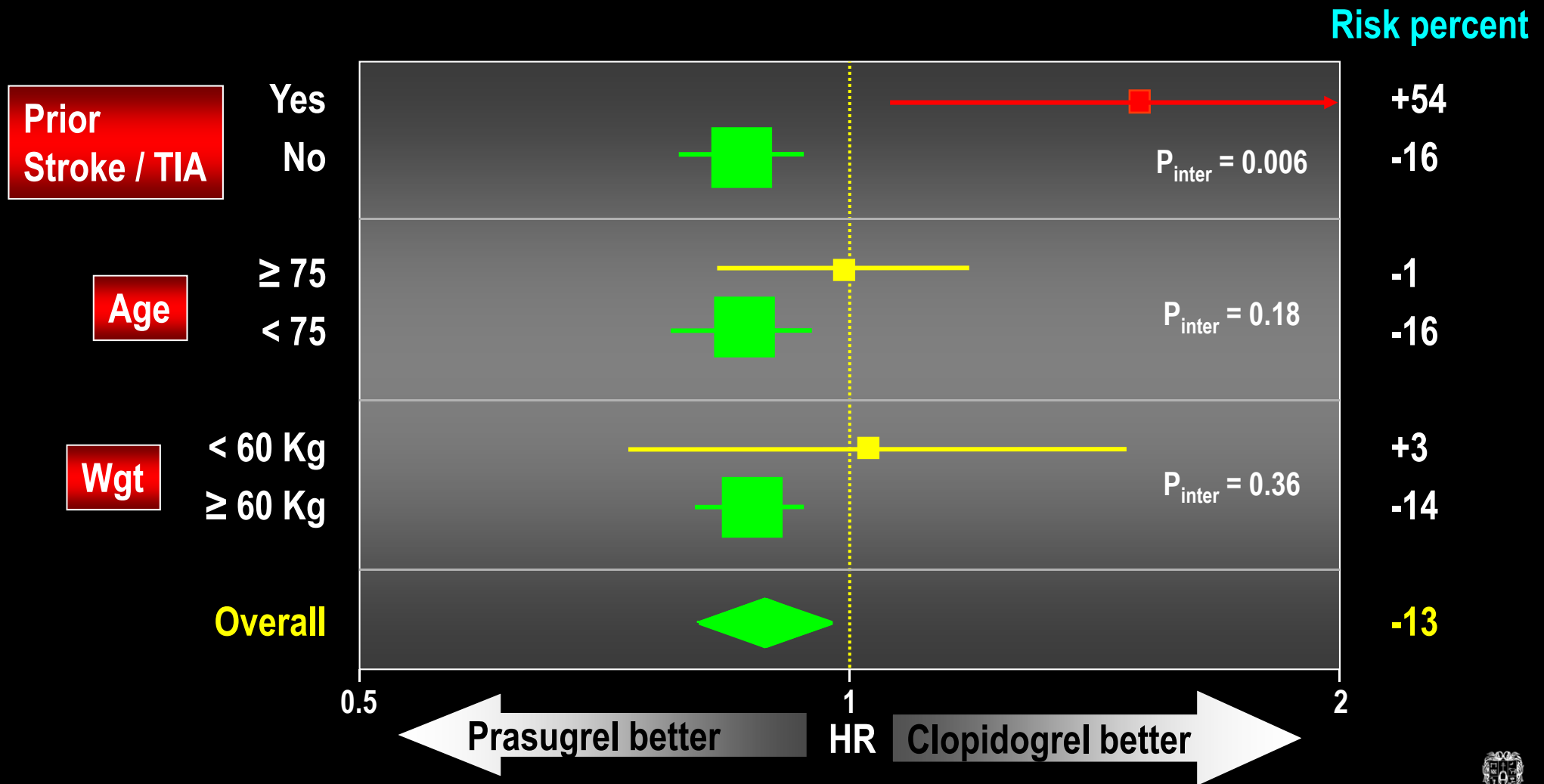
TRITON TIMI-38

TIMI major bleeding



Net Clinical Benefit

Bleeding Risk Subgroups Post-hoc Analysis



ESC/ EACTS Guidelines on myocardial revascularization 2010

Antithrombotic treatment options in myocardial revascularization

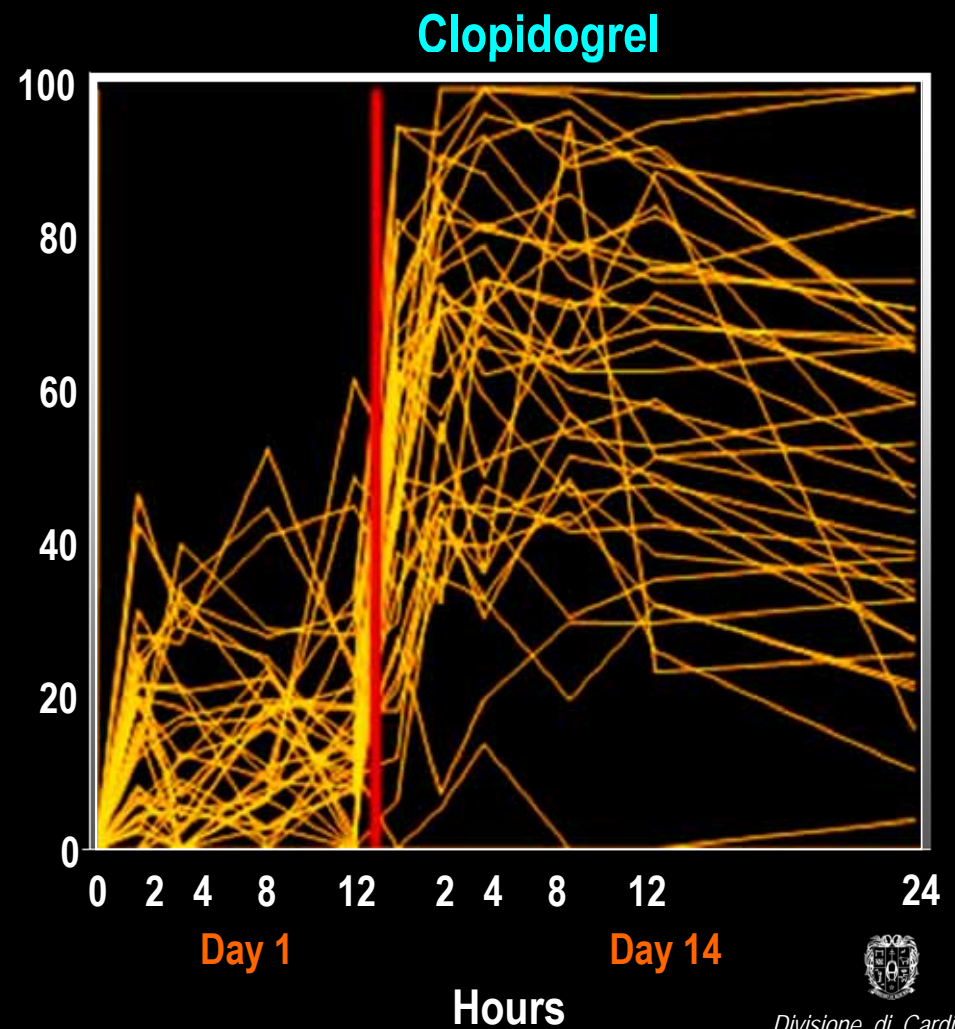
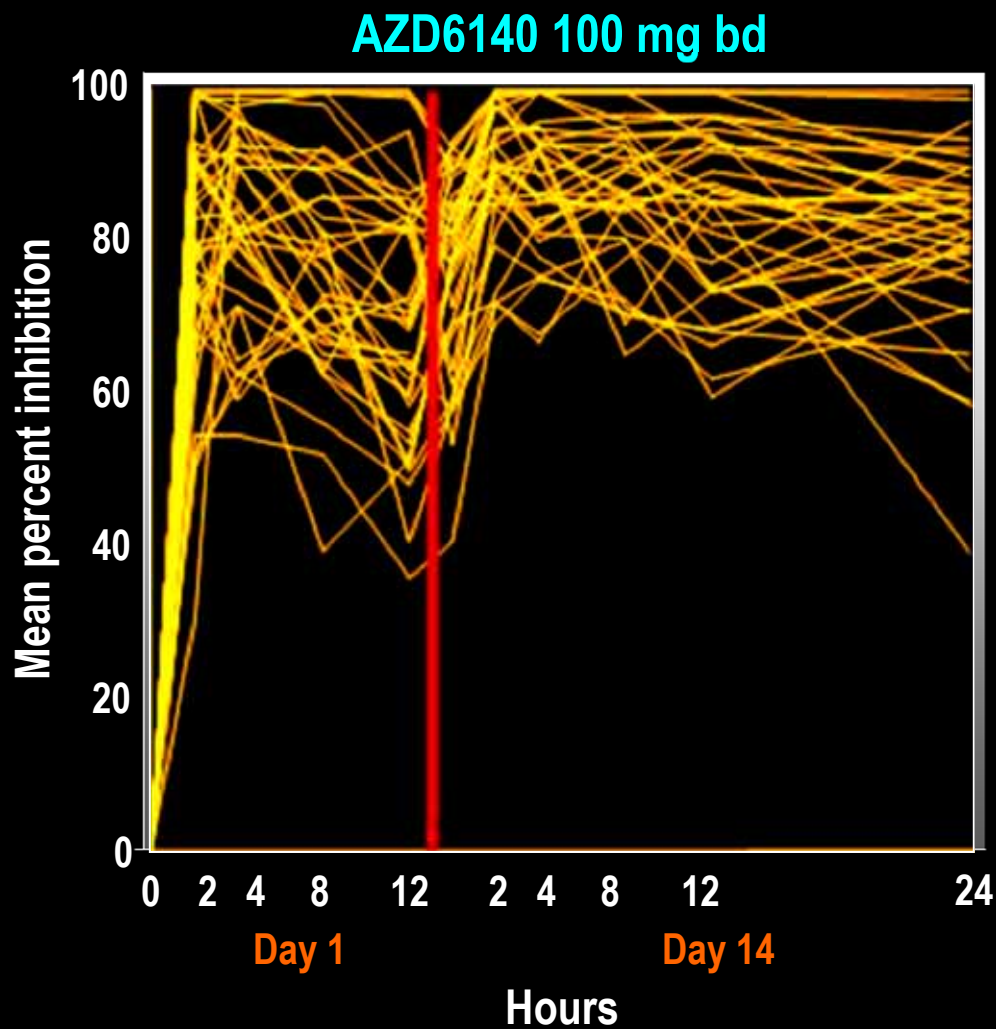
...A predefined subgroup analysis has demonstrated that STEMI patients referred to PCI significantly benefit from ticagrelor vs clopidogrel, with similar bleeding rates.

CLASS I

EVIDENCE B

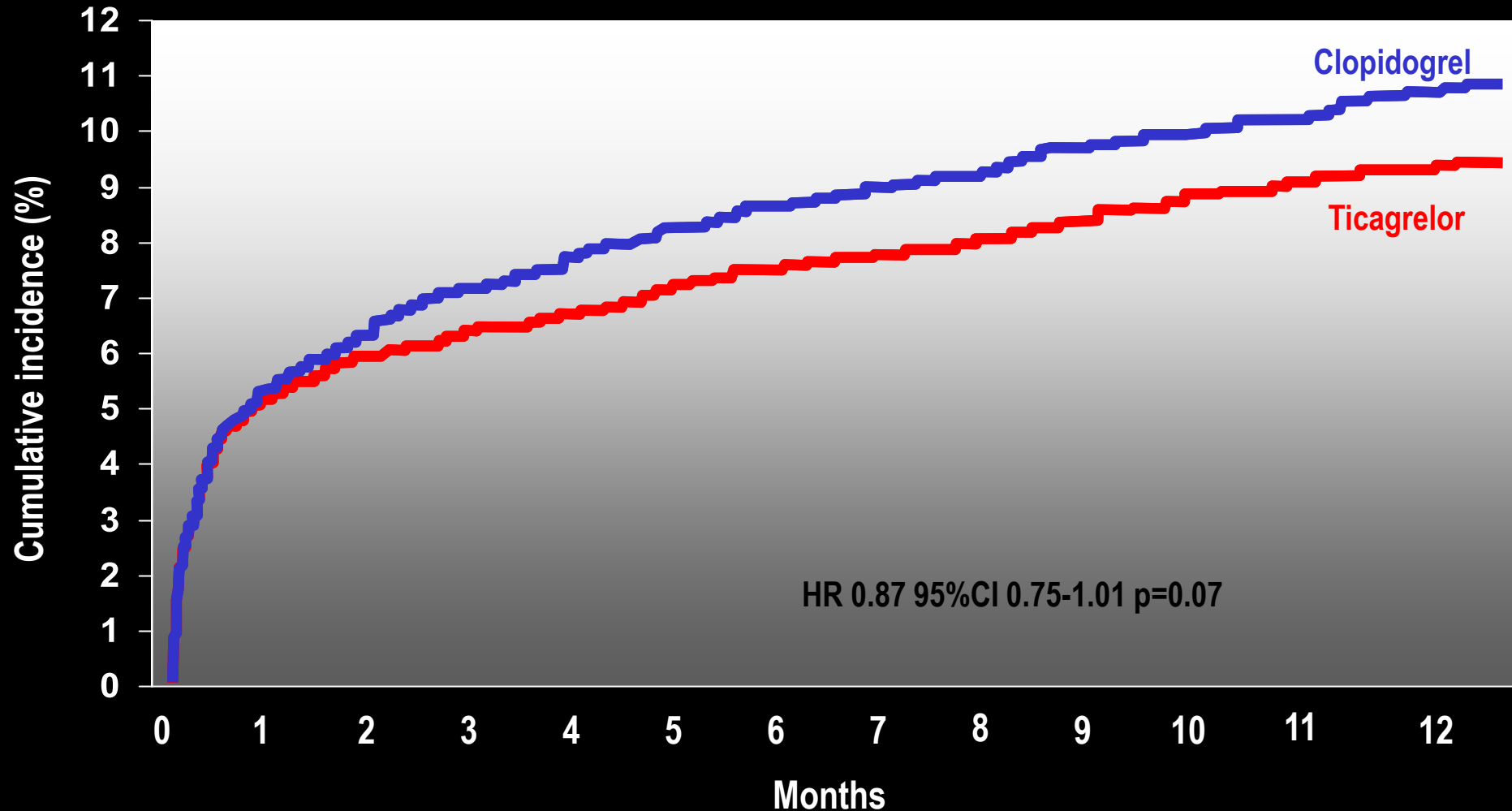
Greater and More Consistent IPA with AZD6140 than Clopidogrel

Final Extent



Ticagrelor vs clopidogrel in STEMI treated with primary PCI

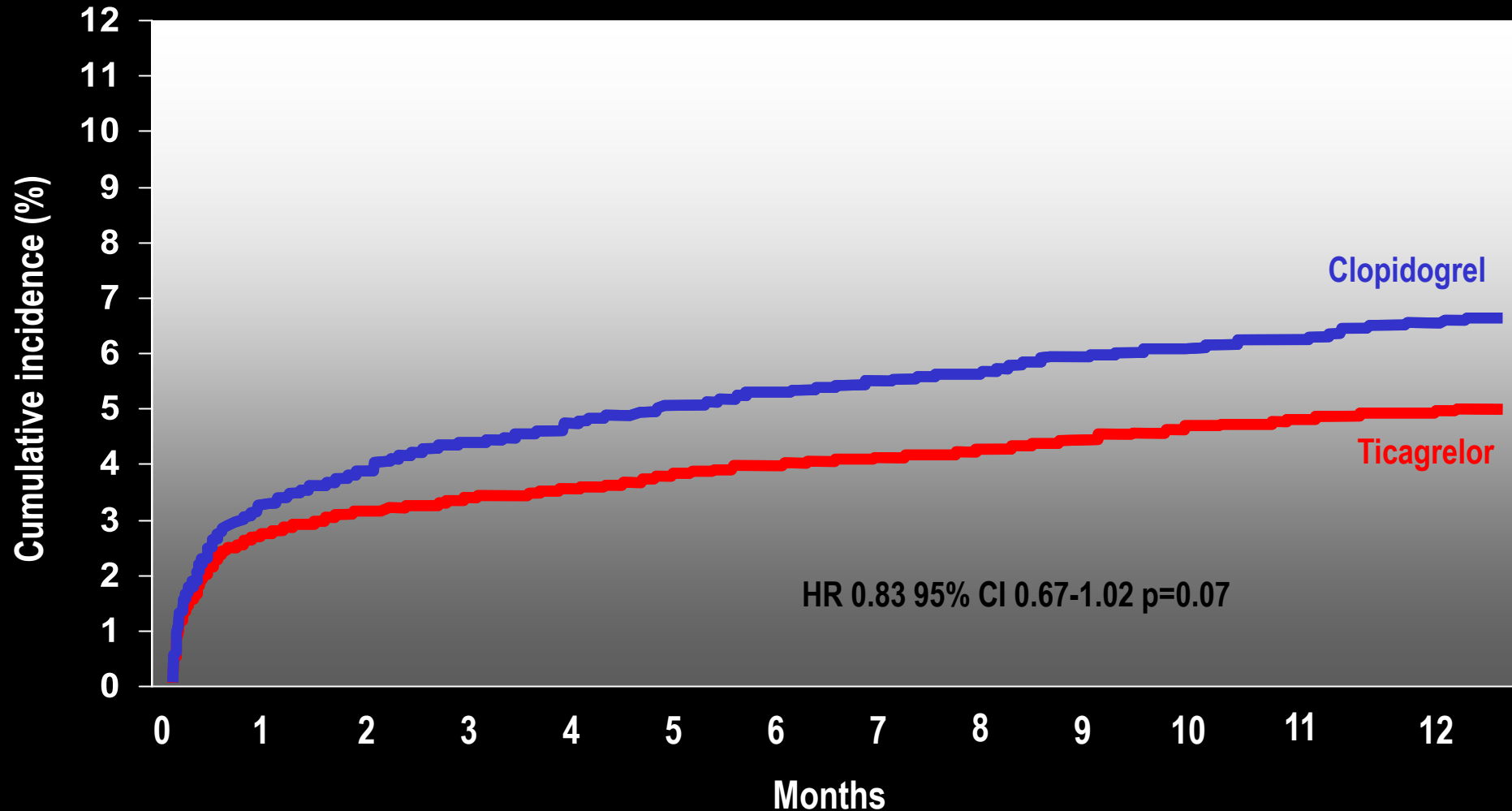
Primary efficacy endpoint



T	3752	3476	3424	3331	2687	2049	1675
C	3792	3501	3438	3356	2726	2097	1679

Ticagrelor vs clopidogrel in STEMI treated with primary PCI

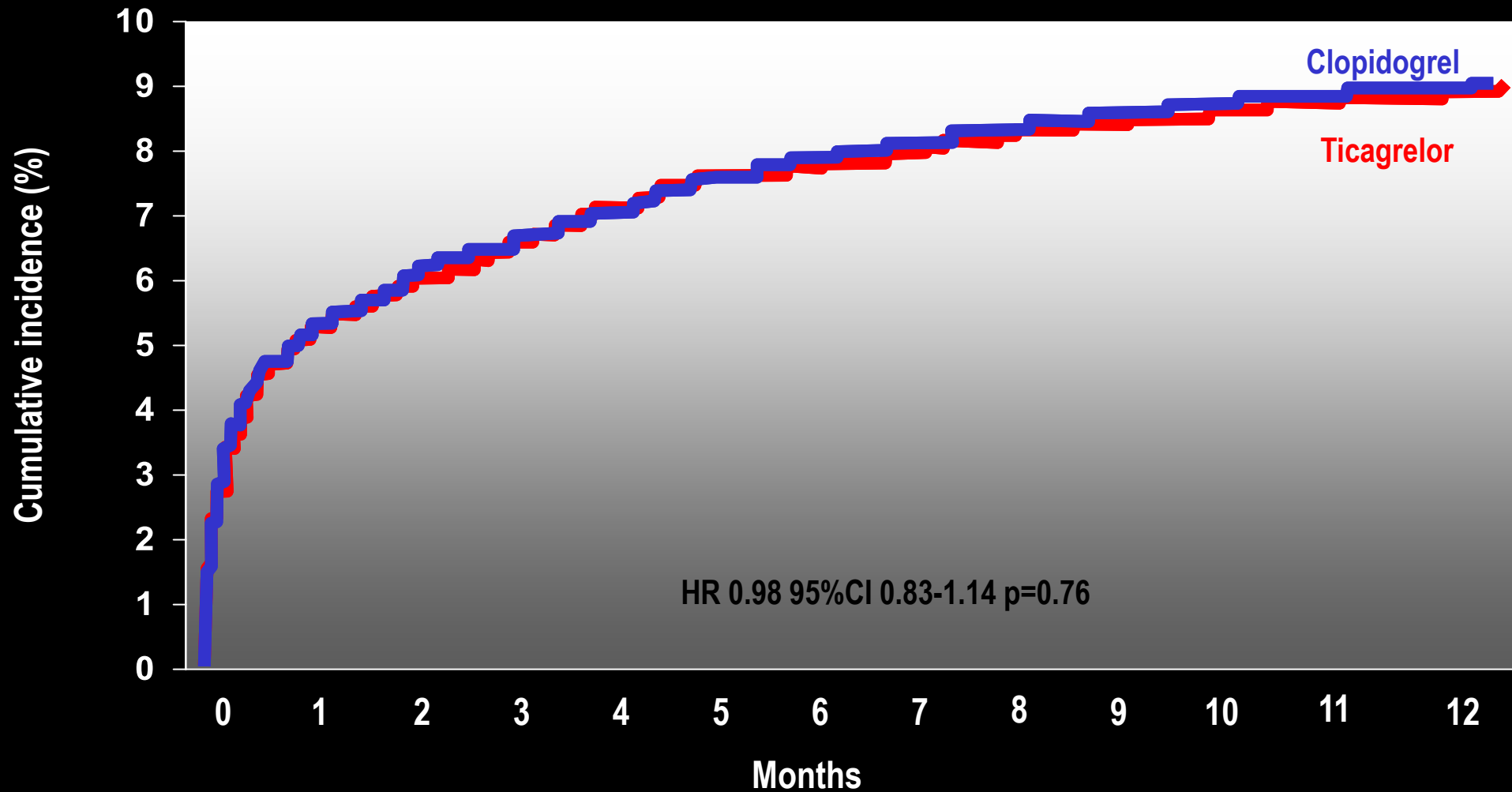
Cardiovascular death



T	3752	3581	3539	3461	2812	2154	1766
C	3792	3614	3580	3511	2872	2216	1773

Ticagrelor vs clopidogrel in STEMI treated with primary PCI

Major bleeding according to PLATO definition



T	3719	3079	2920	2812	2183	1592	1459
C	3752	3092	2972	2850	2202	1624	1471

Pre-hospital vs. In-hospital initiation of ticagrelor therapy in STEMI

ATLANTIC study design

STEMI patients planned for primary PCI
(symptom onset < 6 hours)

(n = 1.770)

R

Randomized, Parallel-group, Double blind, Placebo controlled phase IV trial

Pre-hospital Ticagrelor loading dose (180 mg)
followed by in-hospital matching placebo

Pre-hospital placebo followed by
in-hospital Ticagrelor loading dose (180mg)

Primary endpoint: TIMI flow grade 3 of MI culprit vessel at initial angiography;
ST-segment resolution up to pre PCI >70%

Secondary endpoint: 30-days death, MI, urgent revascularization, stent thrombosis,
life threatening bleeding, major and minor bleeding



PEGASUS TIMI 54 Study design

History of MI 1-3 years prior +
≥ 1 additional atherothrombosis risk factor

Standard background care
(ASA 75-100 mg recommended)

(n = 21,000)

* Age ≥ 65yrs, diabetes, 2nd prior MI, multivessel CAD,
PAD or chronic non-end stage renal dysfunction

Randomize double blind

Ticagrelor 90 mg BID

Ticagrelor 60 mg BID

Placebo

Follow up Visits
Q4 mos for 1st ys, then Q6 mos

Min 12 mos and average 24 mos follow-up

Event driven trial

Primary Efficacy Endpoint: CV death, MI or stroke

Primary Safety Endpoint: TIMI major Bleeding



The cycle of continuous quality improvement

