

Abciximab plus Heparin versus Bivalirudin in Patients with NSTEMI Undergoing PCI

ISAR-REACT 4 Trial

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On behalf of

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Conflicts of interest

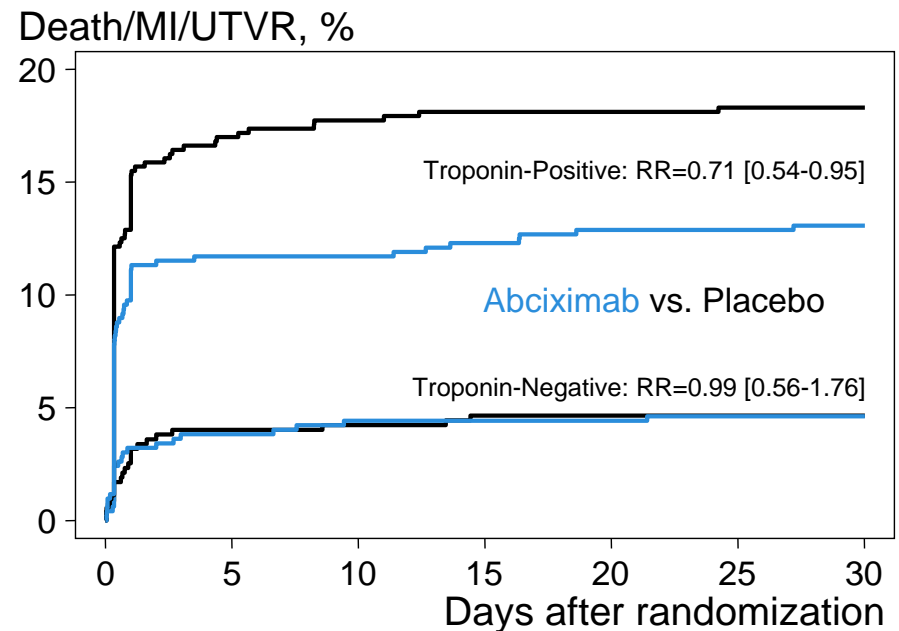
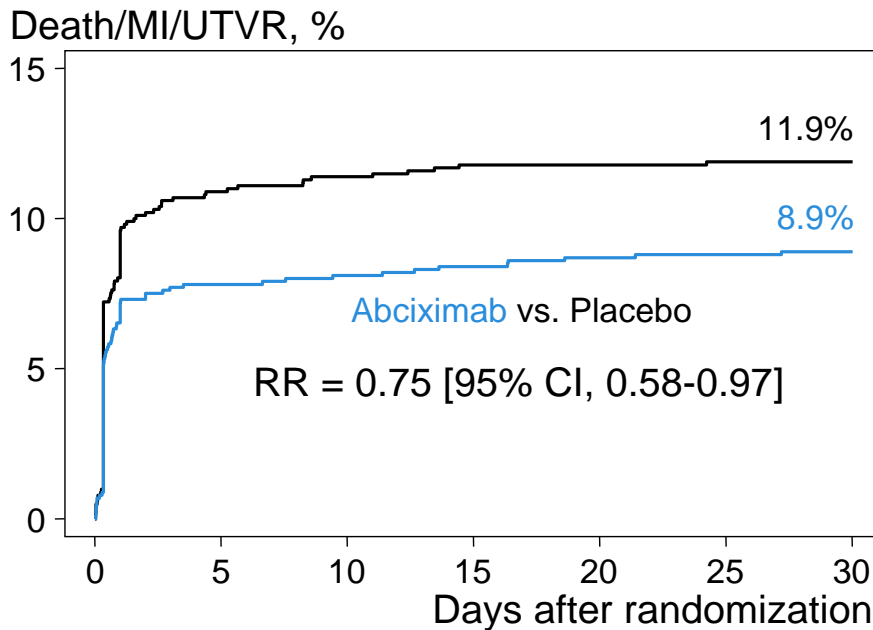
Speaker fees/honoraria from:

- Abbott
- Astra-Zeneca
- Bristol-Myers
- Cordis
- Daichii Sankyo/Lilly
- Medtronic

Background

- Abciximab, a GP IIb/IIIa inhibitor, has improved the results of PCI in patients with ACS

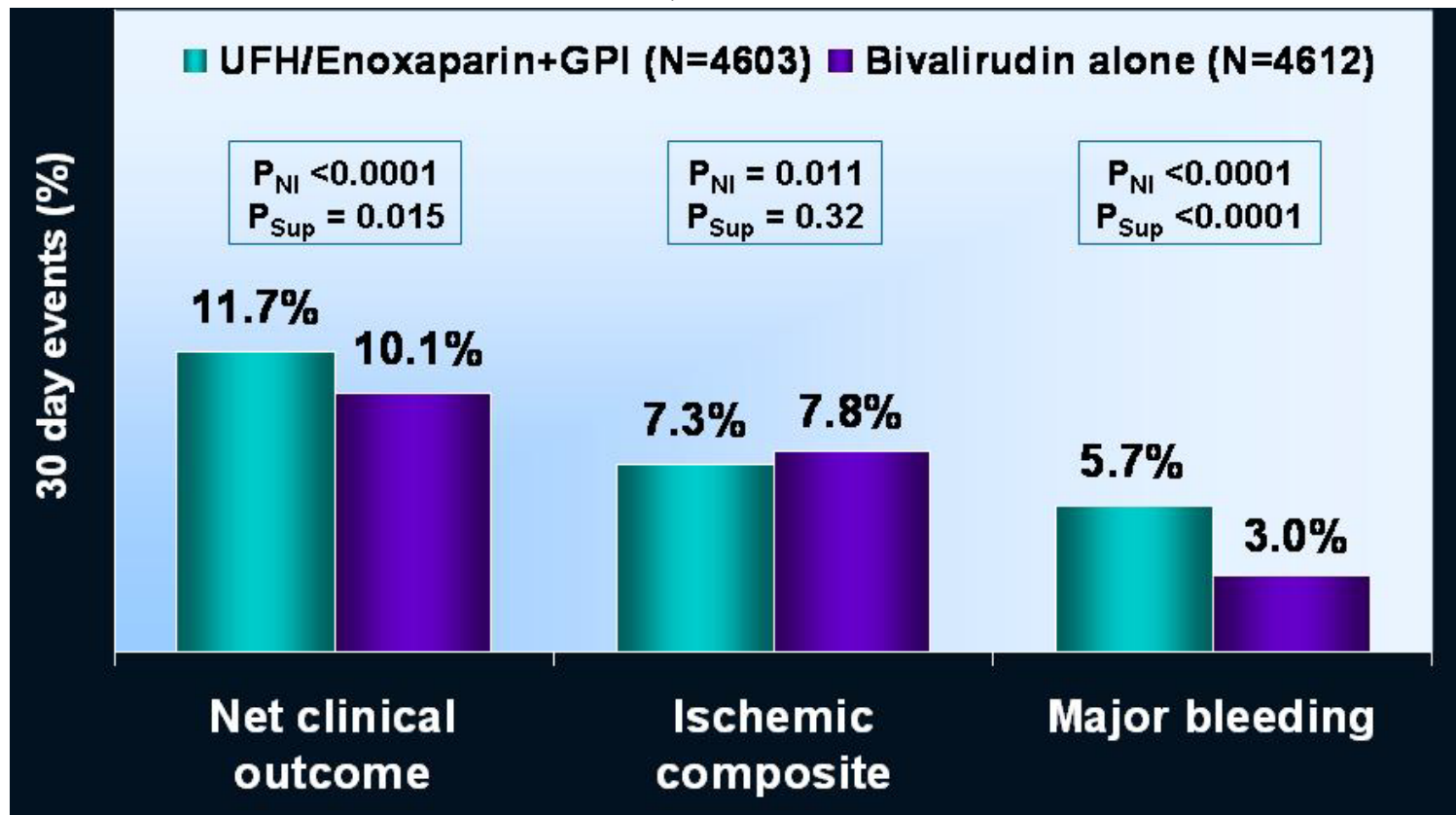
ISAR-REACT 2, JAMA 2006



Background

- Bivalirudin, a direct thrombin inhibitor, has been superior to GP IIb/IIIa inhibitors plus heparins in patients with ACS

ACUITY, NEJM 2006



Background

Relevant issues with the ACUITY trial

- Open-label trial
- 40% of the patients without elevated troponin
- PCI in <60% of the patients
- Control group: a mixture of UFH/Enoxaparin and 3 GP IIb/IIIa inhibitors (only 9% abciximab)
- Liberal definition of bleeding (including 5 cm hematomas)

Rationale of ISAR-REACT 4 trial

The combination of abciximab and unfractionated heparin has not been compared with bivalirudin in dedicated studies involving patients with NSTEMI undergoing PCI

Objective of ISAR-REACT 4 trial

to determine whether the combination of abciximab with unfractionated heparin, as compared with bivalirudin, improves the clinical outcomes in patients with acute NSTEMI undergoing PCI

Study organization

Steering committee:

A. Schömig (Chairman), A. Kastrati (PI), F.J. Neumann, P.B. Berger

Participating centers:

Germany

- Deutsches Herzzentrum, Munich (PI: S. Massberg)
- Herz-Zentrum, Bad Krozingen (PI: F.J. Neumann)
- 1. Med. Klinik, Klinikum rechts der Isar, Munich (PI: K.L. Laugwitz)
- Vivantes Auguste-Viktoria-Klinikum, Berlin (PI: H. Schühlen)
- Uniklinik, Tübingen (PI: M. Gawaz)
- Vivantes Klinikum Neukölln, Berlin (PI: H. Darius)

US

- Geisinger Clinic, Danville, PA (PI: P.B. Berger)

Italy

- Careggi Hospital, Florence (PI: D. Antoniucci)

Inclusion criteria

- Age between 19 and 80 years;
- unstable angina within the preceding 48 hours;
- elevated levels of cardiac biomarkers (troponin or CK MB);
- and coronary stenoses requiring PCI

Main exclusion criteria

- STEMI within 48 hours from symptom onset;
- cardiogenic shock;
- active bleeding or a bleeding diathesis;
- a planned staged PCI procedure within 30 days;
- glomerular filtration rate <30 ml/min or creatinine >30 mg/L;
- receipt of coumarin within 7d, a GP IIb/IIIa inhibitor within 14d, UFH within 4h, LMWH within 8 h, and bivalirudin within 24h

Primary endpoint

A composite of death, large myocardial infarction or urgent target vessel revascularization within 30 days

(large MI: new Q waves or CK-MB elevation >5 times above ULN)

Secondary endpoints

Efficacy

A composite of death, any myocardial infarction or urgent target vessel revascularization within 30 days

(any MI: new Q waves or CK-MB elevation >3 times above ULN)

Safety

Major bleeding within 30 days

(intracranial, intraocular, or retroperitoneal; Hb decrease >40g/L plus either overt bleeding or need for transfusion of 2 or more units)

Sample size calculation

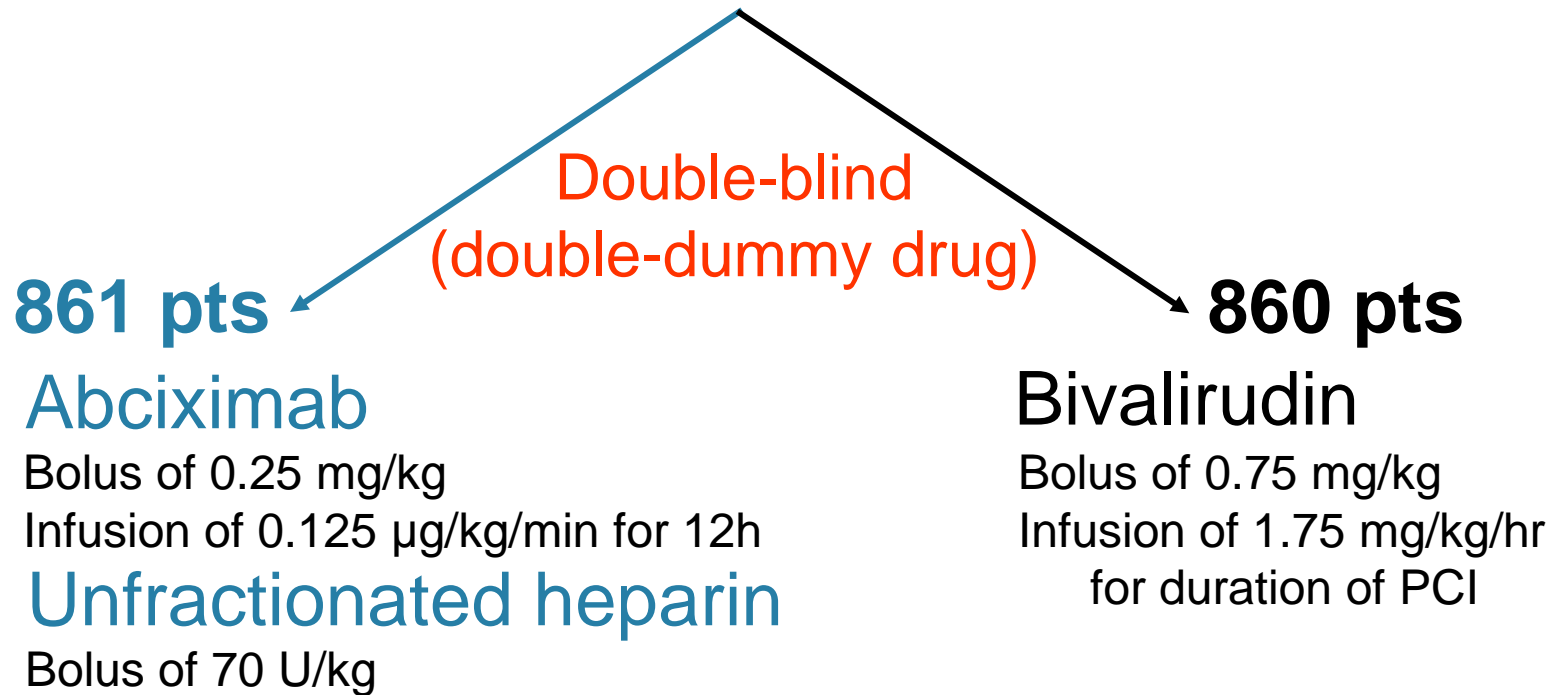
- 30% reduction of the incidence of the 1° endpoint with abciximab plus heparin
 - abciximab plus heparin: 10.7%
 - bivalirudin: 15.3%
- 2-sided α -level: 5%
- Power: 80%

1,700 patients

Trial flow-chart

1,721 Pts with NSTEMI

Pre-treated with 600 mg of clopidogrel



No PCI: 2 patients

2 patients

Baseline characteristics

	Abciximab n=861	Bivalirudin n=860
Age, yrs	67.5 11.2	67.5 10.8
Women, %	23.2	23.1
Hypercholesterolemia, %	69.7	67.4
Arterial hypertension, %	86.5	84.5
Diabetes mellitus, %	29.8	28.3
Current smoker, %	25.0	22.7
Body mass index, kg/m ²	27.8 4.6	27.8 4.2

Baseline characteristics

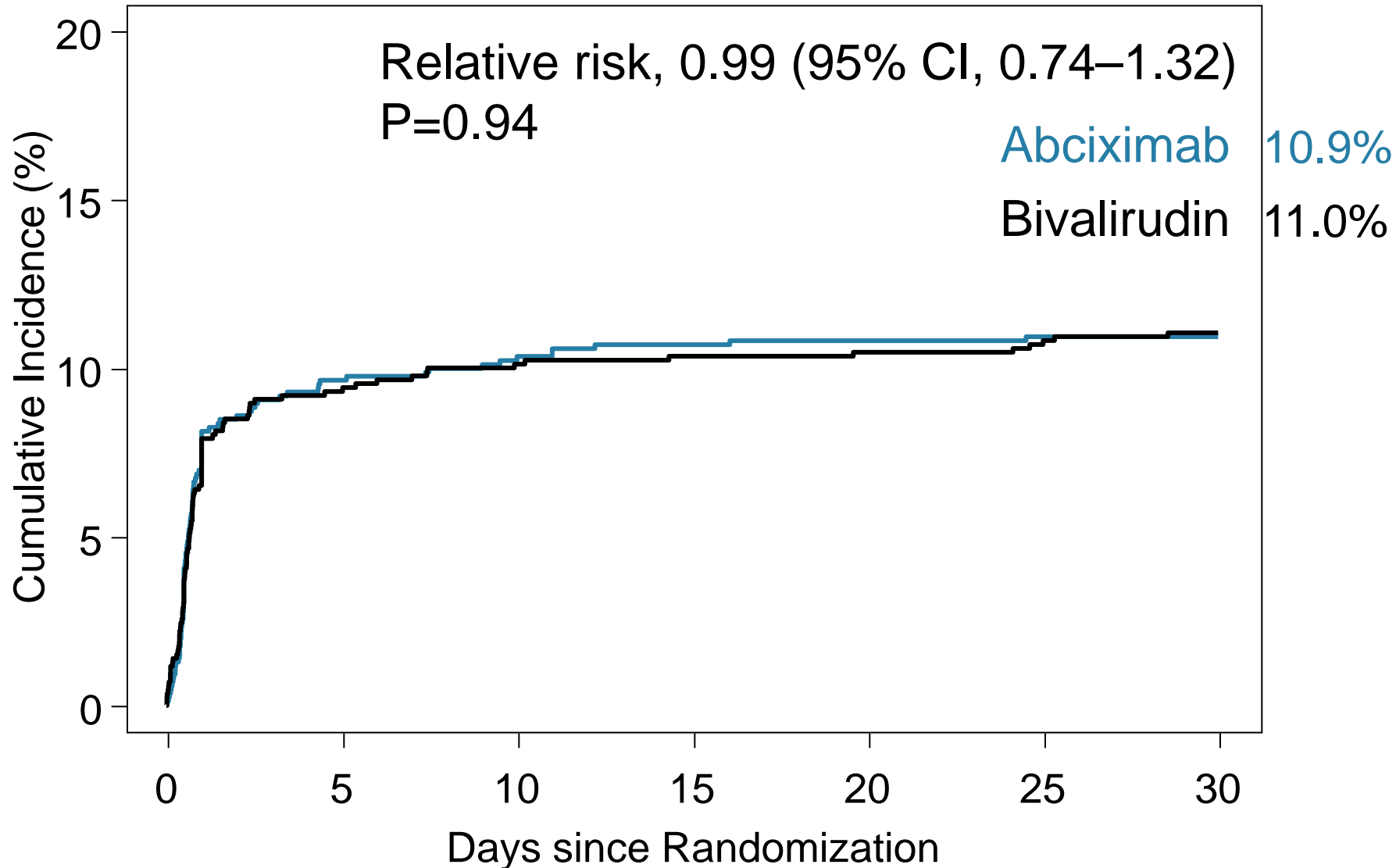
	Abciximab n=861	Bivalirudin n=860
Previous PCI, %	33.9	31.0
Previous CABG, %	10.7	10.3
Previous MI, %	21.8	19.0
Multivessel disease, %	80.6	79.4
LV ejection fraction, %	51.5 11.5	51.3 11.5

Lesion and procedure characteristics

	Abciximab n=859	Bivalirudin n=858
Vessel		
LCA, %	3.1	2.9
LAD, %	36.8	40.4
LCx, %	28.1	26.9
RCA, %	27.5	26.5
Bypass vein graft, %	4.5	3.3
Complex (B2/C) lesions, %	85.2	87.2
DES, %	88.9	88.2
BMS, %	6.8	7.6
PTCA, %	4.3	4.2

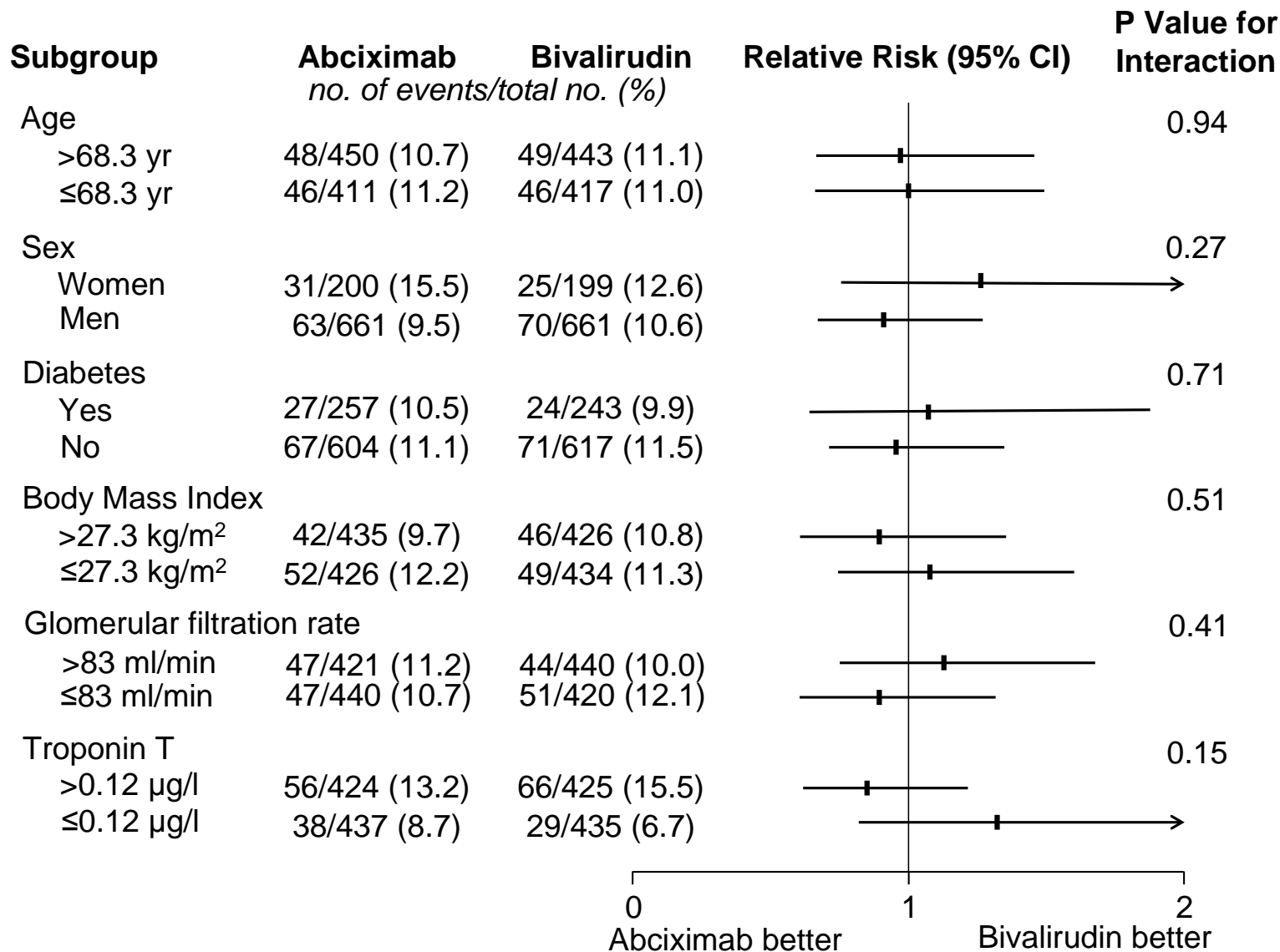
Primary endpoint

Death, large MI, uTVR, major bleeding



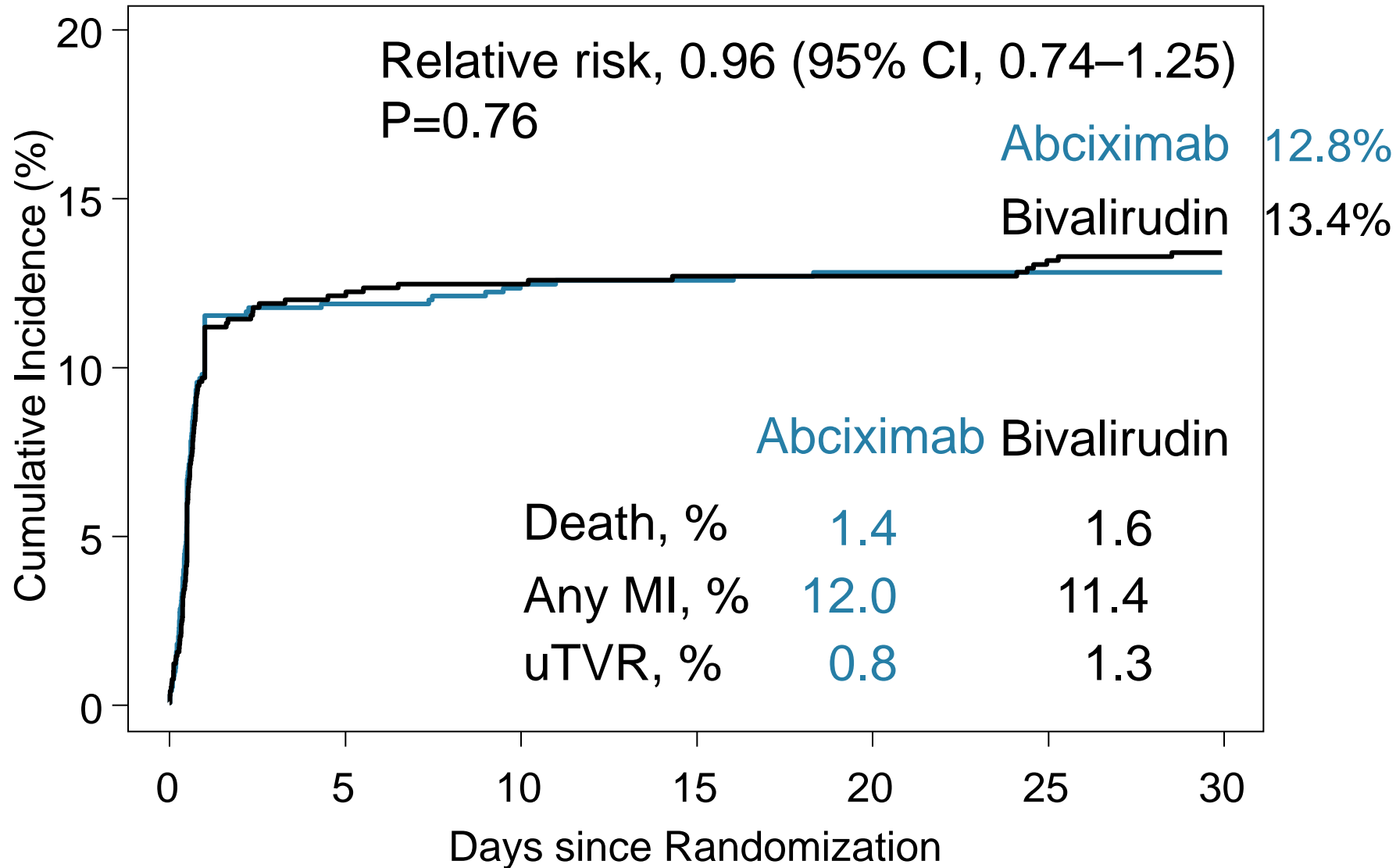
Primary endpoint analysis in various subsets

Death, large MI, uTVR, major bleeding



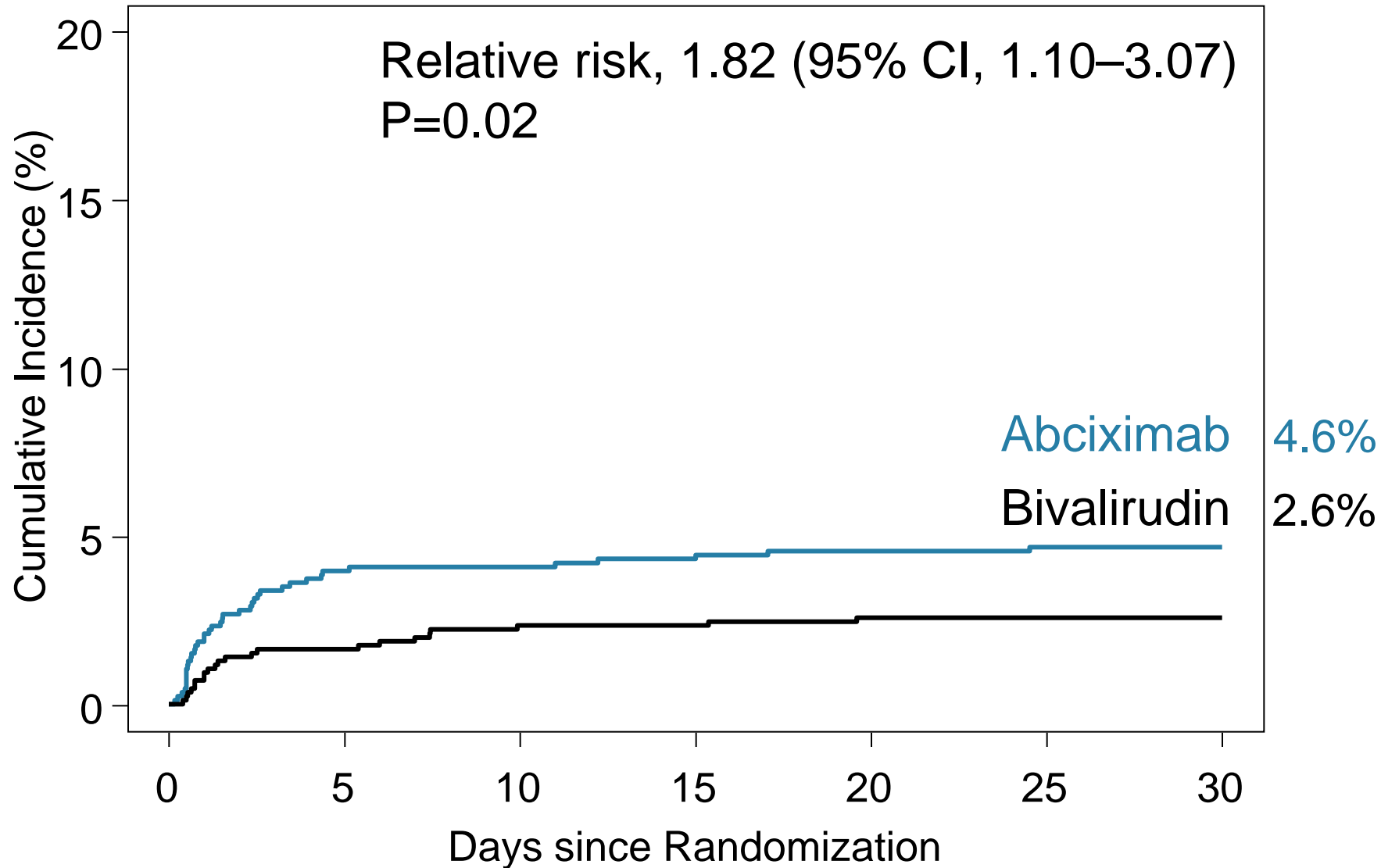
Secondary efficacy endpoint

Death, any MI, uTVR



Secondary safety endpoint

Major bleeding



Conclusions

Abciximab and unfractionated heparin, as compared with bivalirudin, failed to reduce the rate of the primary endpoint and increased the risk of bleeding among patients with NSTEMI undergoing PCI.

These findings along with those reported for STEMI show that bivalirudin might be the preferred drug in patients undergoing PCI for an acute myocardial infarction, with or without ST-segment elevation.

Online publication

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Abciximab and Heparin versus Bivalirudin for Non–ST-Elevation Myocardial Infarction

Adnan Kastrati, M.D., Franz-Josef Neumann, M.D., Stefanie Schulz, M.D., Steffen Massberg, M.D., Robert A. Byrne, M.B., B.Ch., Miroslaw Ferenc, M.D., Karl-Ludwig Laugwitz, M.D., Jürgen Pache, M.D., Ilka Ott, M.D., Jörg Hausleiter, M.D., Melchior Seyfarth, M.D., Michael Gick, M.D., David Antoniucci, M.D., Albert Schömig M.D., Peter B. Berger, M.D., and Julinda Mehilli, M.D., for the ISAR-REACT 4 Trial Investigators*