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# Abciximab in Patients with AMI Undergoing Primary PCI After Clopidogrel Pretreatment

## **BRAVE-3 Trial**

***Bavarian Reperfusion Alternatives Evaluation-3 Trial***

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**BRAVE-3**

## **Financial Disclosure**

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**No financial relationship to disclose**

## Background

- Glycoprotein IIb/IIIa inhibitors (GPI) may improve the results of primary PCI in acute STEMI
- Pretreatment with a 300mg loading dose of clopidogrel improved the outcome of patients undergoing primary PCI in the setting of the CLARITY trial
- A higher, 600mg loading dose of clopidogrel further enhances and accelerates platelet inhibition

## Objective

..to assess whether abciximab further reduces the infarct size in patients with acute ST-elevation myocardial infarction undergoing primary PCI after pre-treatment with 600 mg clopidogrel

# Inclusion Criteria

- Patients with acute ST-elevation myocardial infarction presenting within 24 hours from the onset of symptoms
  - chest pain lasting more than 20 min
  - $\geq 0.1$  mV of ST-segment elevation in  $\geq 2$  limb leads or  $\geq 0.2$  mV in  $\geq 2$  contiguous precordial leads or new left bundle branch block on surface ECG
  
- Written, informed consent

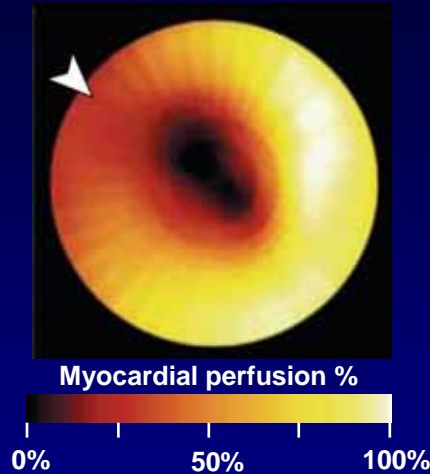
# Exclusion Criteria

- Age > 80 or < 18 years
- Malignancies with a life expectancy <1 year
- Cardiogenic shock or prolonged cardiopulmonary resuscitation
- Increased risk of bleeding
  - Previous stroke within the last 3 months
  - Active bleeding or bleeding diatheses
  - Recent trauma or major surgery within the last 30 days
  - Suspected aortic dissection
  - Recent use of GPI within 14 days
  - Oral anticoagulation therapy with coumarin derivatives
  - Severe uncontrolled hypertension (>180mmHg, unresponsive to therapy)
- Relevant hematologic deviations
  - (hemoglobin < 100g/L or hct < 34%, platelet count < 100 x 10<sup>9</sup>/L)
- Coronary intervention within the last 30 days
- Known allergy to study medication, Pregnancy, Prior inclusion in the study

# Endpoints

## Primary endpoint:

- Final infarct size  
(% of the left ventricle)



SPECT study  
(5-7 days after  
randomization)

## Secondary endpoints:

- Death
- Myocardial reinfarction
- Urgent revascularization
- Stroke
- Major and minor bleeding (TIMI criteria)
- Profound thrombocytopenia

# Sample Size Calculation

## Assumptions:

- Infarct size of the LV in placebo group:  $16.9\% \pm 13.9\%$
- Reduction of infarct size with abciximab by 20%
- $\alpha$ -level: 0.05 (two-sided);  $\beta$ -error: 0.10

## Sample size:

- 353 patients per group with SPECT study
- to accommodate for possible missing SPECT studies:  
400 patients per group planned

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|                               |             |
|-------------------------------|-------------|
| Study Chair:                  | A. Schömig  |
| Study Principal Investigator: | A. Kastrati |
| Data Co-ordinator:            | J. Mehilli  |

# Study Therapy

## BRAVE-3 (randomized, double-blind)

Clopidogrel 600 mg oral  
Aspirin 500 mg i.v. or oral  
Unfractionated Heparin 5000 IU

### Abciximab

n=401

Bolus: 0.25 mg/kg

Infusion: 0.125 µg/kg/min/12h

### Placebo

n=399

Additional UFH bolus of 70U/kg

Placebo infusion for 12h

Aspirin 200mg/day indefinitely  
Clopidogrel 2 x 75mg/day for 3 days  
Clopidogrel 75mg/day for at least 4 weeks

**BRAVE-3**

# Baseline Characteristics

|                                    | Abciximab<br>(n=401) | Placebo<br>(n=399) |
|------------------------------------|----------------------|--------------------|
| Age, yrs                           | 62.4±11.7            | 61.8±12.2          |
| Women, %                           | 24                   | 27                 |
| Hypercholesterolemia, %            | 42                   | 44                 |
| Arterial hypertension, %           | 70                   | 71                 |
| Diabetes mellitus, %               | 19                   | 16                 |
| Current smoker, %                  | 42                   | 41                 |
| Body mass index, kg/m <sup>2</sup> | 27.1±3.8             | 27.0±4.1           |
| Previous MI, %                     | 10                   | 11                 |
| Previous CABG, %                   | 4                    | 2                  |
| Mean±SD                            |                      |                    |

BRAVE-3

# Infarct Characteristics

|                               | Abciximab<br>(n=401) | Placebo<br>(n=399) |
|-------------------------------|----------------------|--------------------|
| Infarct localization, %       |                      |                    |
| anterior                      | 42                   | 44                 |
| inferior                      | 43                   | 43                 |
| lateral                       | 15                   | 13                 |
| Killip Class, %               |                      |                    |
| I                             | 76                   | 77                 |
| II                            | 18                   | 18                 |
| III                           | 4                    | 3                  |
| IV                            | 2                    | 2                  |
| Arterial blood pressure, mmHg |                      |                    |
| systolic                      | 138±23               | 139±22             |
| diastolic                     | 79±13                | 80±14              |
| Heart rate, beats/min         | 73±17                | 73±16              |
| Mean±SD or %                  |                      |                    |

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## Time Intervals

|                            | Abciximab<br>(n=401) | Placebo<br>(n=399) |
|----------------------------|----------------------|--------------------|
| Symptom to admission       | 210[110;420]         | 216[110;467]       |
| Admission to study drug    | 25[15;43]            | 20[14;40]          |
| Clopidogrel loading to PCI | 73[54;104]           | 75[53;105]         |
| Admission to PCI           | 78[59;109]           | 80[58;110]         |

Median [25<sup>th</sup>, 75<sup>th</sup> percentiles] in minutes

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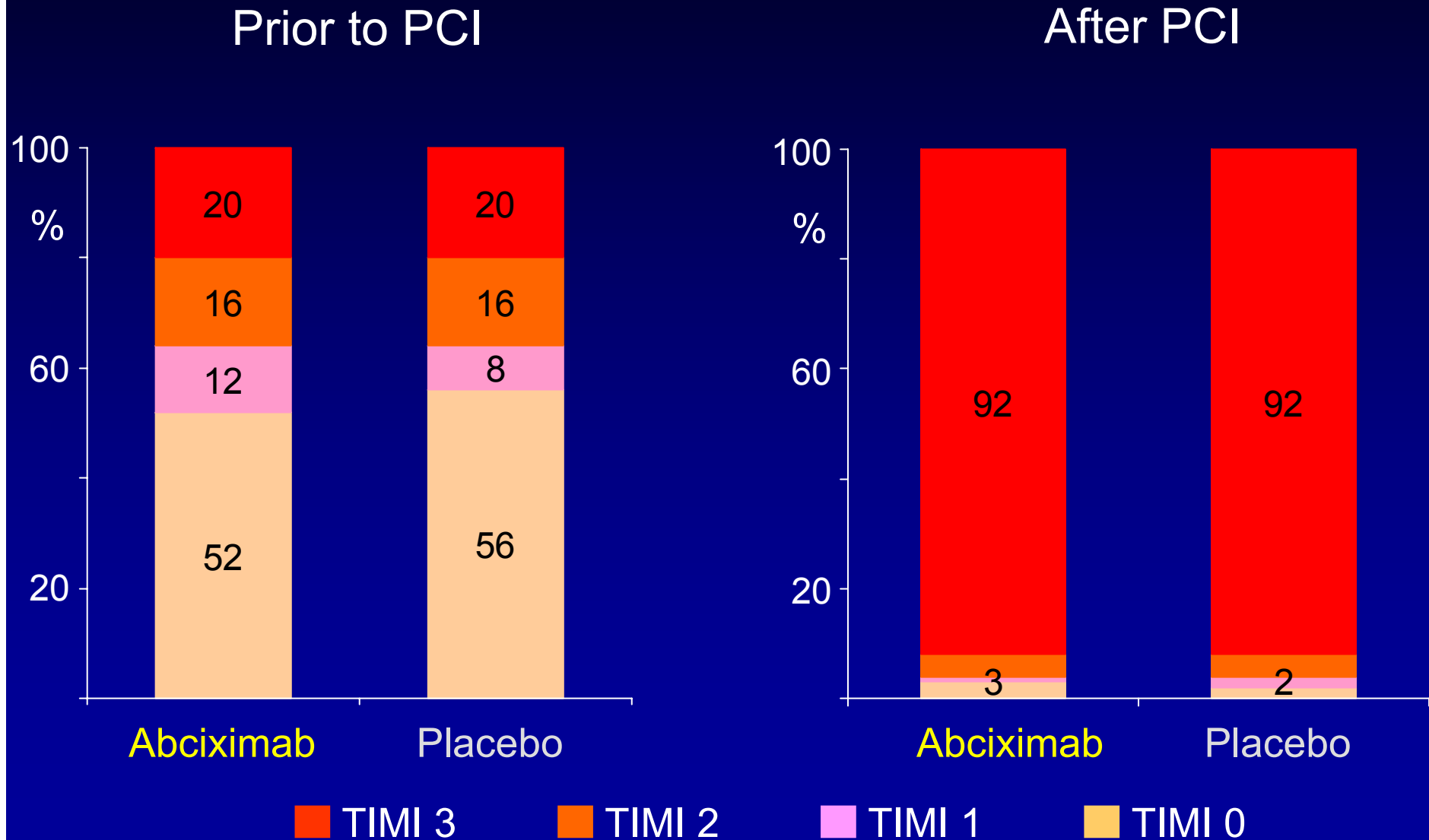
## Angiographic Characteristics

|                                    | Abciximab<br>(n=401) | Placebo<br>(n=399) |
|------------------------------------|----------------------|--------------------|
| LV- ejection fraction, %           | 47.7±11.5            | 48.0±10.6          |
| Multivessel disease, %             | 65                   | 61                 |
| Infarct related coronary artery, % |                      |                    |
| LAD                                | 43                   | 45                 |
| LCx                                | 16                   | 15                 |
| RCA                                | 39                   | 38                 |
| LMA                                | 0                    | 1                  |
| Bypass graft                       | 2                    | 1                  |

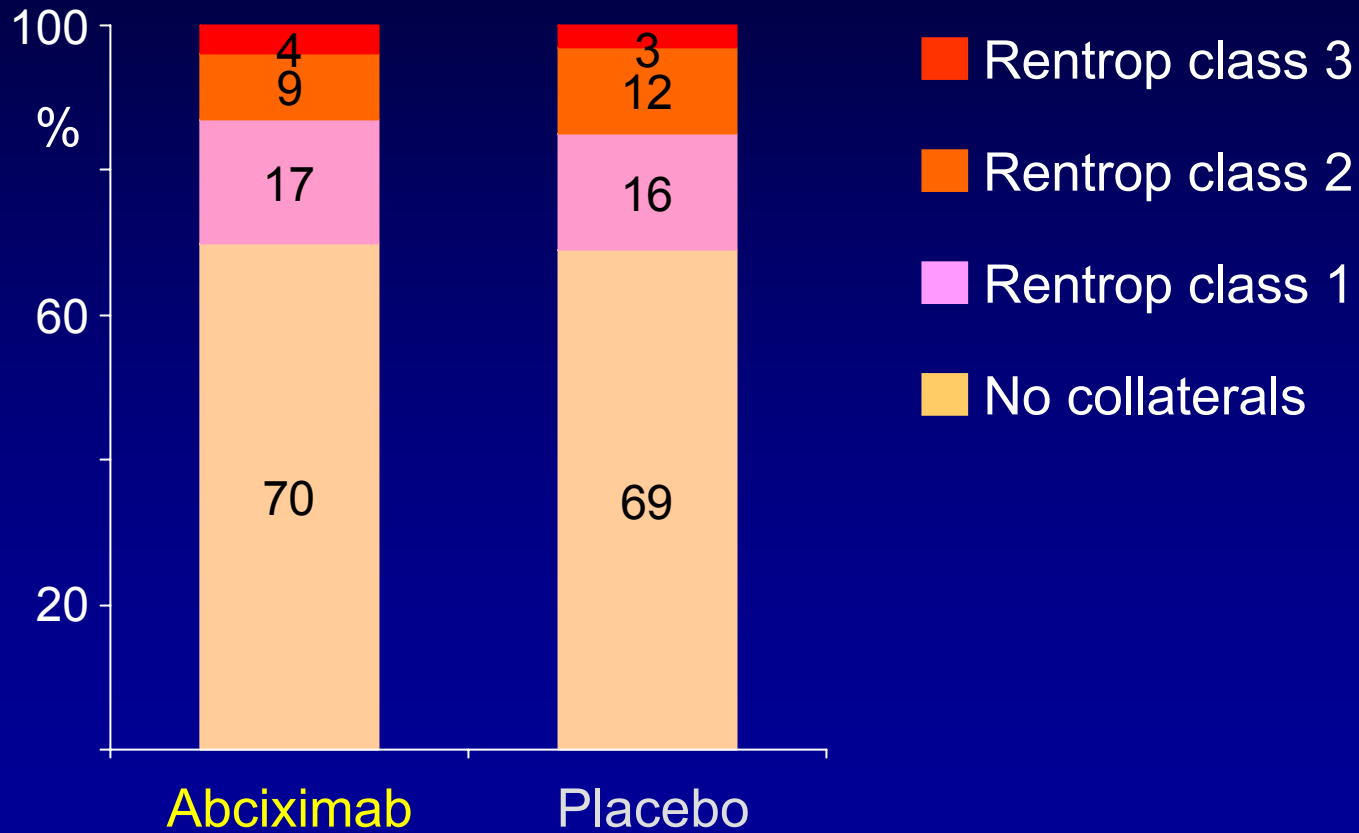
Mean±SD

# Infarct-Related Artery TIMI Flow Rates

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# Collateral Distribution

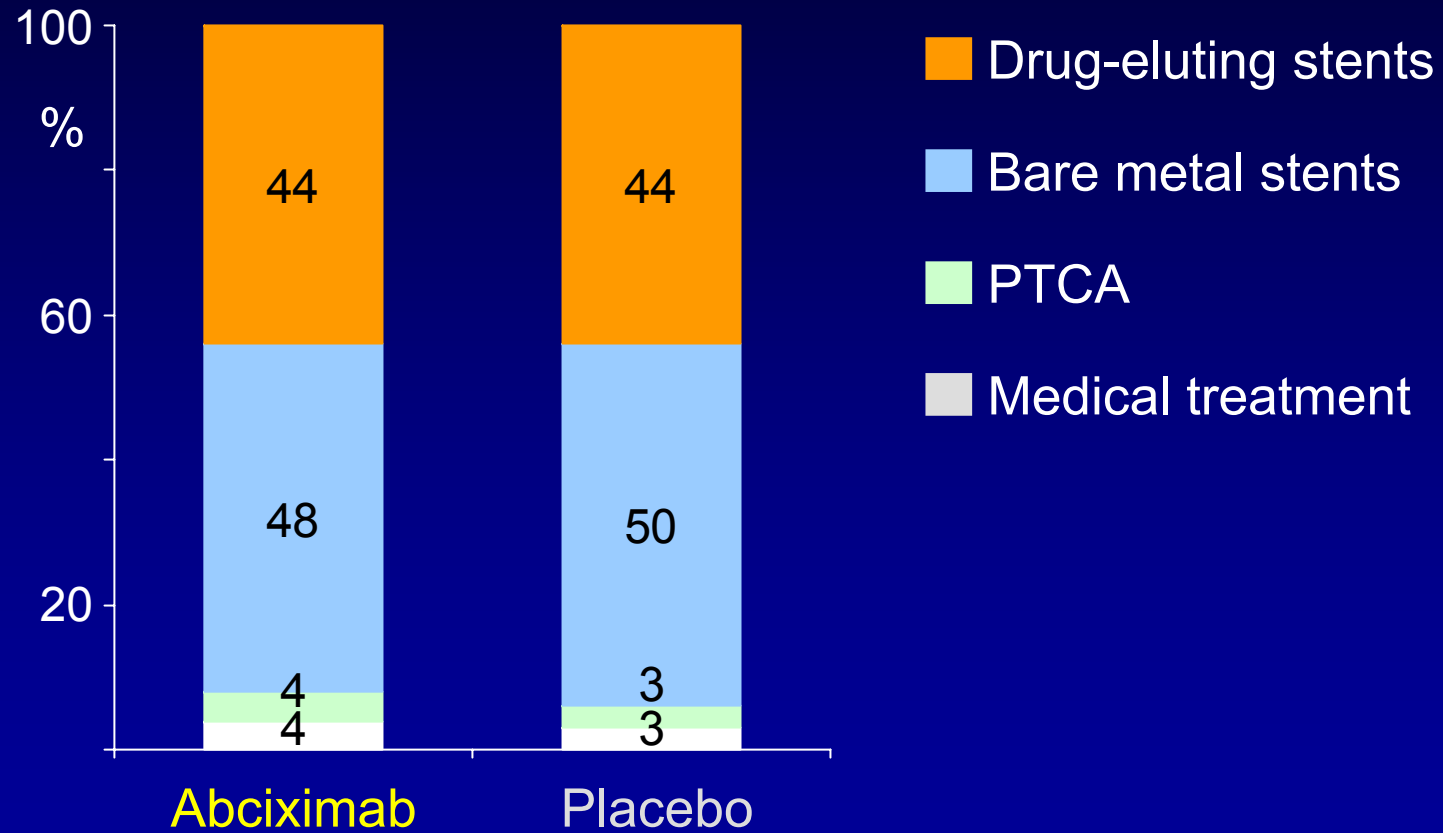


IRA TIMI Flow rate <2

## QCA Measurements

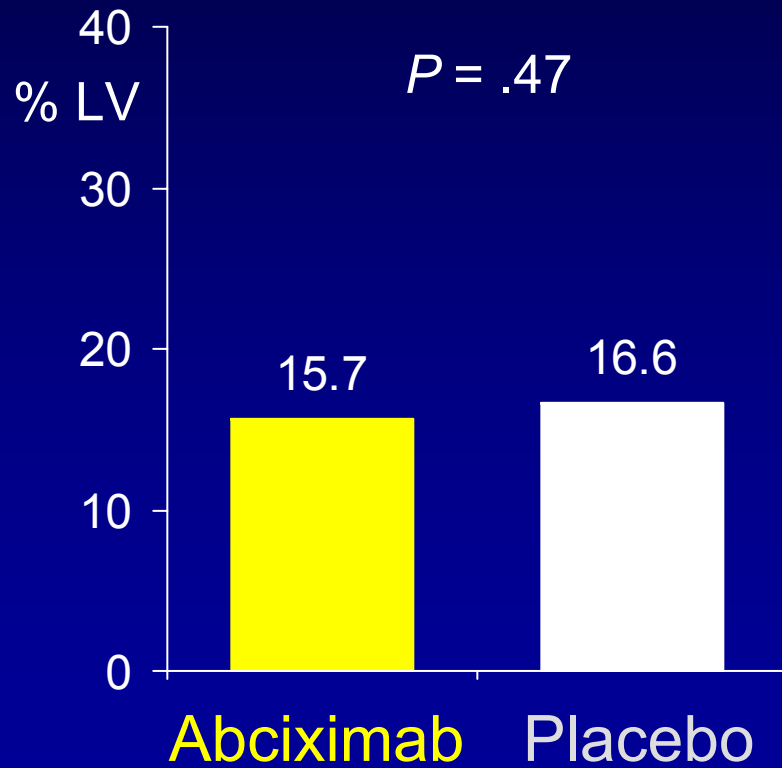
|                               | Abciximab<br>(n=401) | Placebo<br>(n=399) |
|-------------------------------|----------------------|--------------------|
| Vessel size, mm               | 2.93±0.54            | 2.91±0.56          |
| MLD prior PCI, mm             | 0.46±0.56            | 0.44±0.57          |
| DS prior PCI, %               | 84.1±19.4            | 84.3±20.6          |
| Balloon diameter, mm          | 3.26±0.53            | 3.26±0.52          |
| Balloon-to-vessel ratio       | 1.11±0.09            | 1.12±0.12          |
| Maximal balloon pressure, atm | 13.5±2.6             | 13.4±2.5           |
| MLD after PCI, mm             | 2.62±0.67            | 2.63±0.65          |
| DS after PCI, %               | 13.8±16.4            | 13.6±15.2          |
| Mean±SD                       |                      |                    |

# Reperfusion Strategy

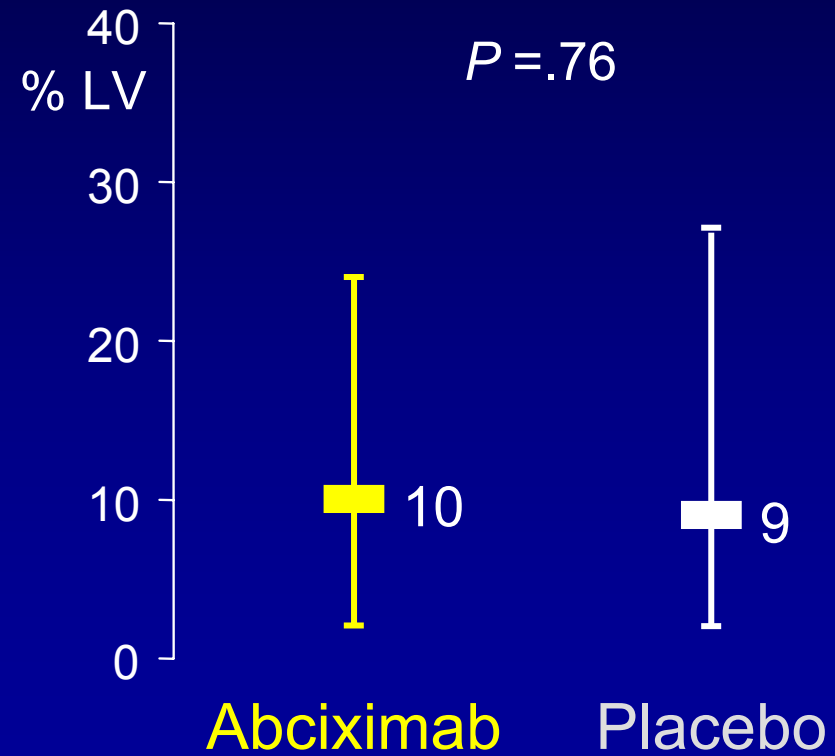


# Primary Endpoint

Final infarct size  
Mean



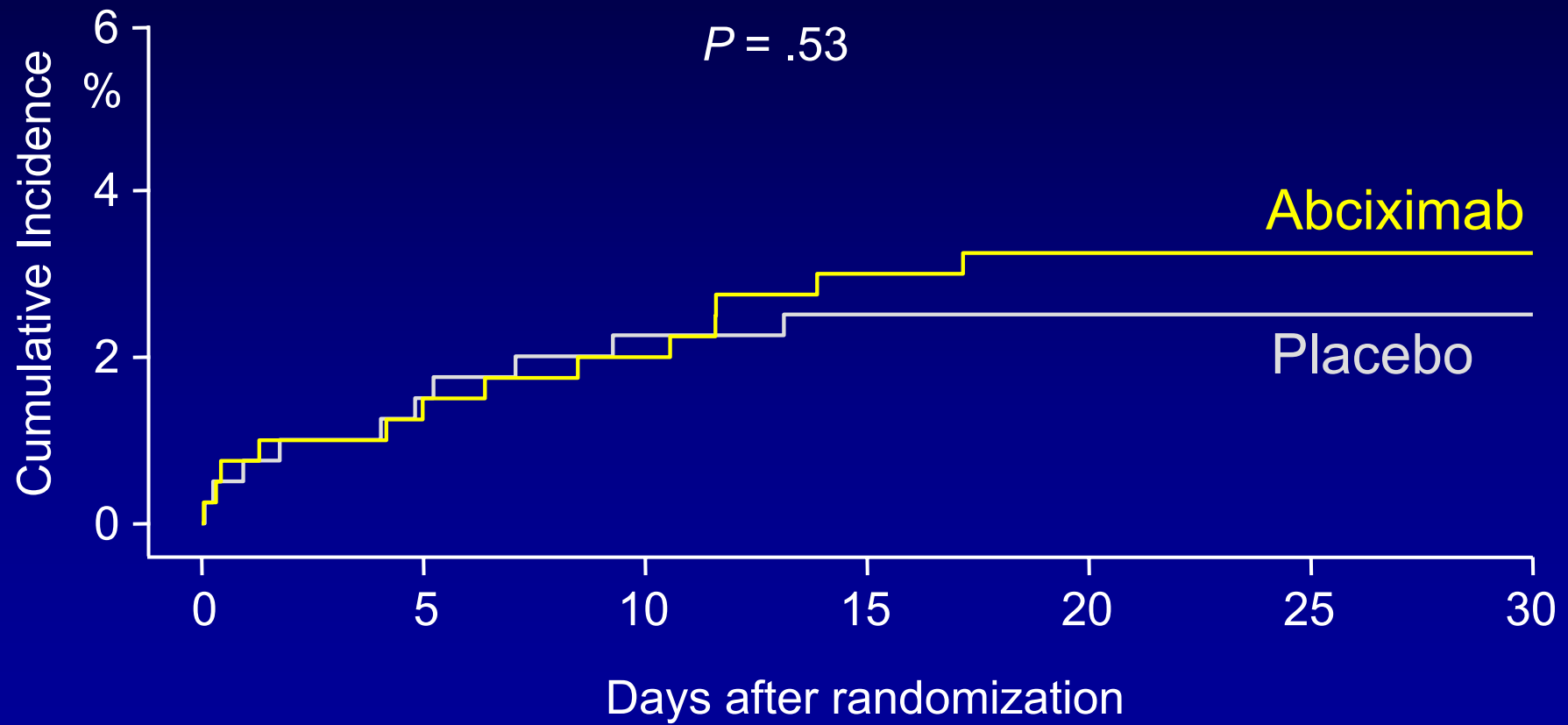
Final infarct size  
Median [25th; 75th percentile]





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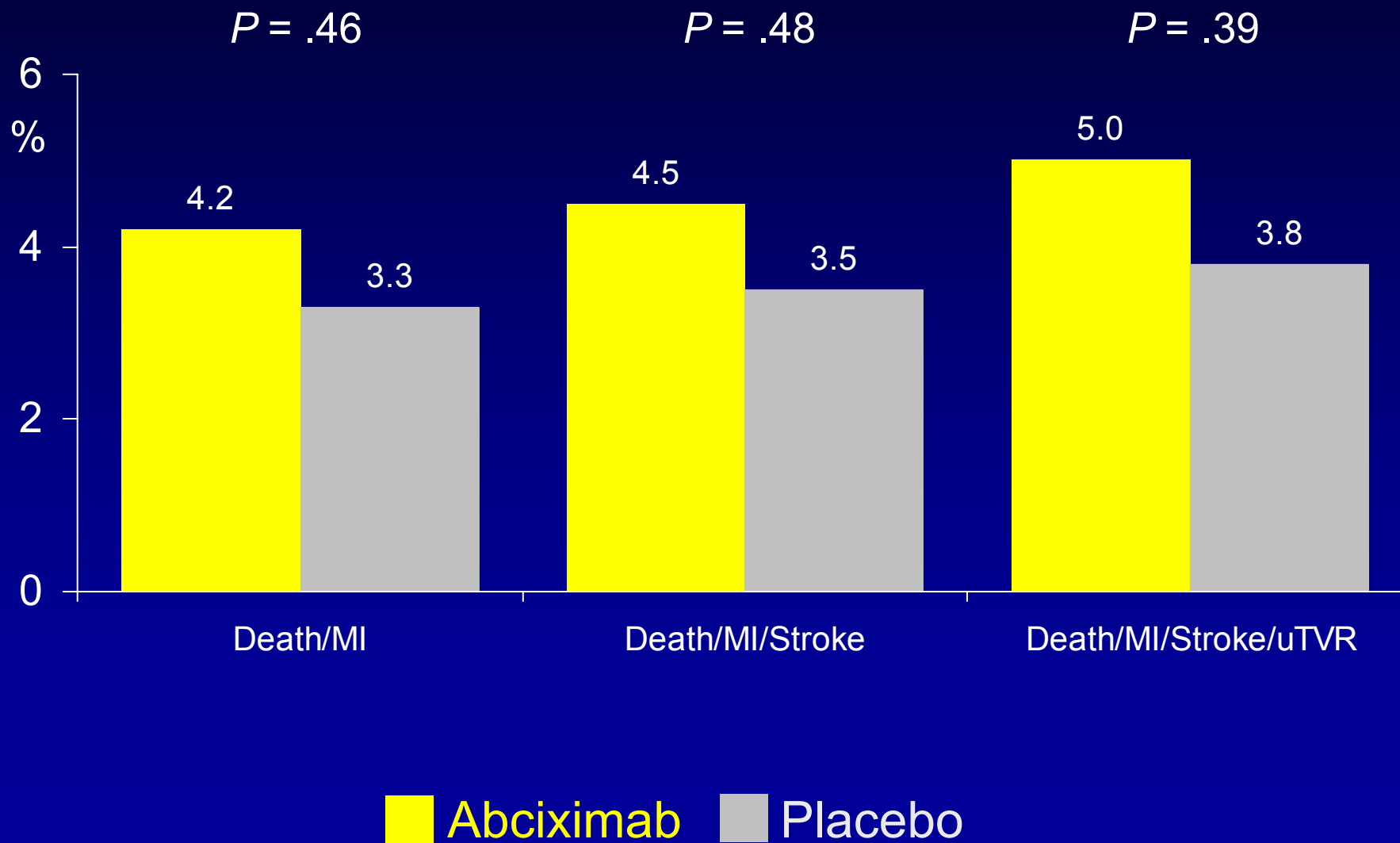
# 30-Day Mortality



# Clinical Adverse Events

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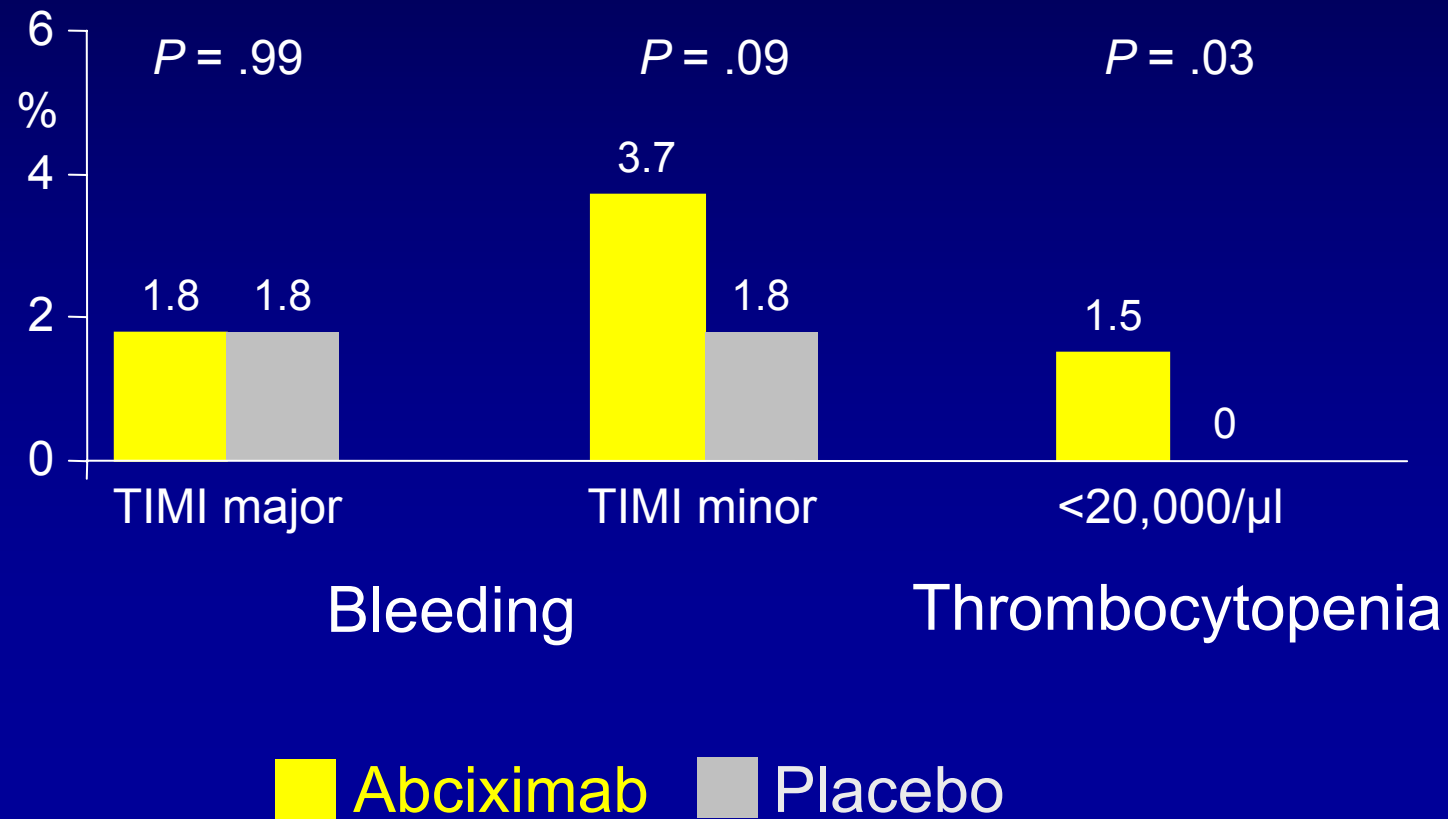
- 30 days -



# Clinical Adverse Events

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- 30 days -



## Conclusion

In patients with acute STEMI undergoing primary PCI after pre-treatment with a 600mg loading dose of clopidogrel, the additional use of abciximab is not associated with further reduction in infarct size