

New Insights From:
**TRial to Assess Improvement in
Therapeutic Outcomes by Optimizing
Platelet Inhibition N with Prasugrel
(TRITON – TIMI 38)**

Stephen D. Wiviott MD
Investigator, TIMI Study Group
Cardiovascular Division
Brigham and Women's Hospital
Assistant Professor of Medicine
Harvard Medical School

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Disclosures:

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Dr. Wiviott:

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ACS (STEMI or UA/NSTEMI) & Planned PCI

ASA ↓ **N= 13,600**

Double-blind

CLOPIDOGREL
300 mg LD/ 75 mg MD

PRASUGREL
60 mg LD/ 10 mg MD

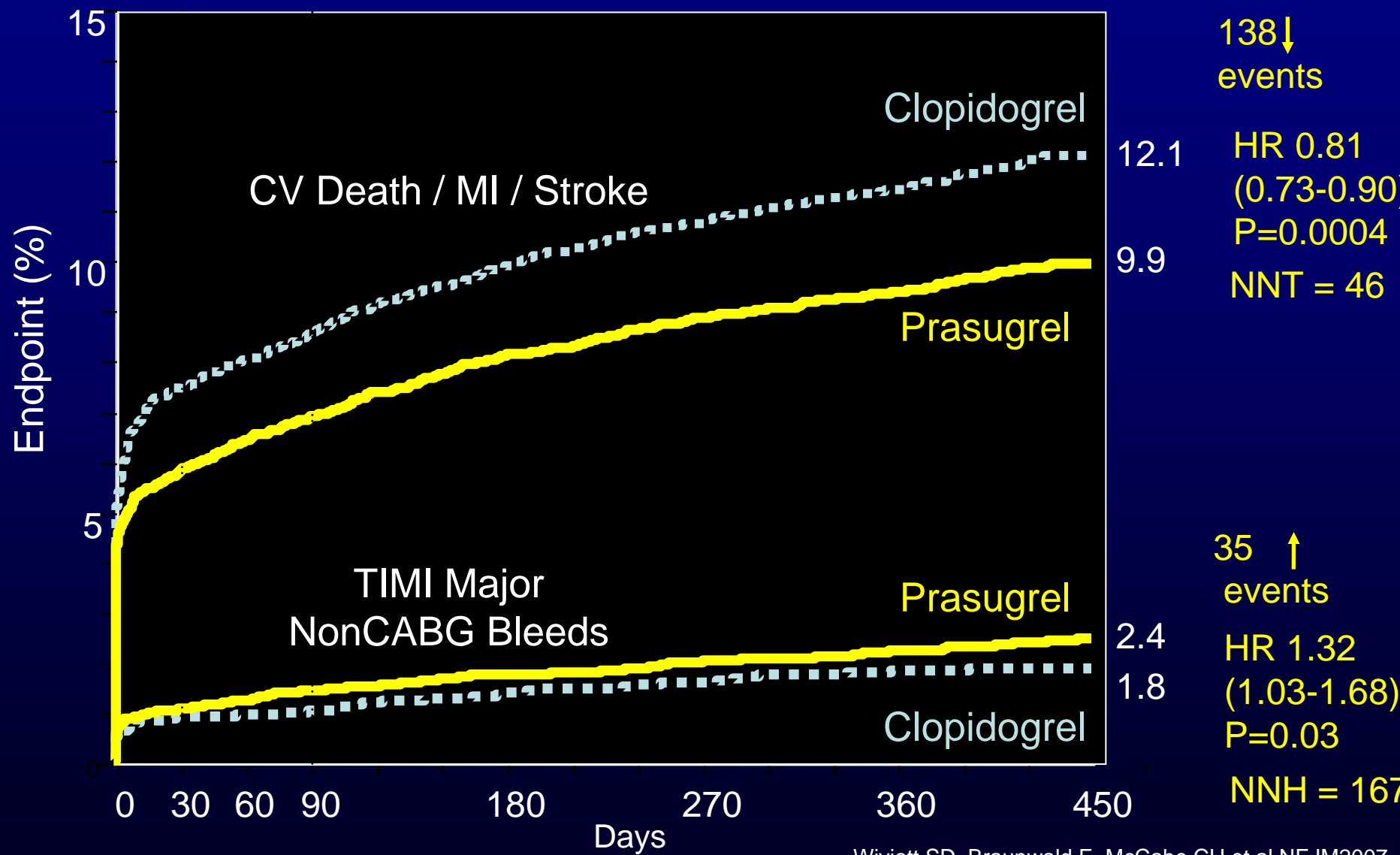
Median duration of therapy - 12 months

1° endpoint: CV death, MI, Stroke

**2° endpoints: CV death, MI, Stroke, Rehosp-Rec Isch
CV death, MI, UTVR
Stent Thrombosis (ARC definite/prob.)**

Safety endpoints: TIMI major bleeds, Life-threatening bleeds

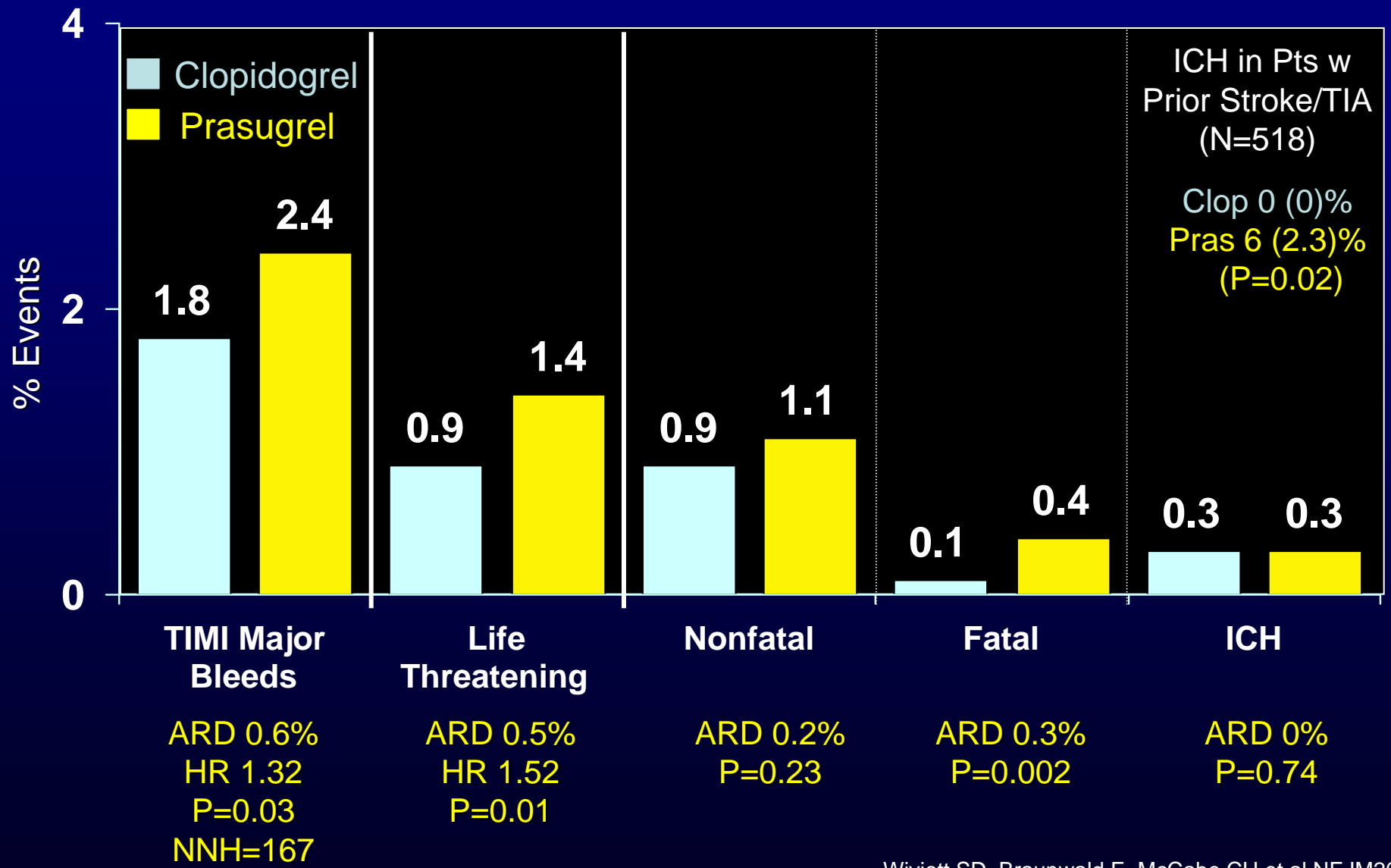
Balance of Efficacy and Safety



Bleeding Events

Safety Cohort

(N=13,457)



Timing

Antman EM, JACC 2008

Diabetes

Wiviott SD, Circulation 2008

STEMI

Montalescot G, ESC 2008

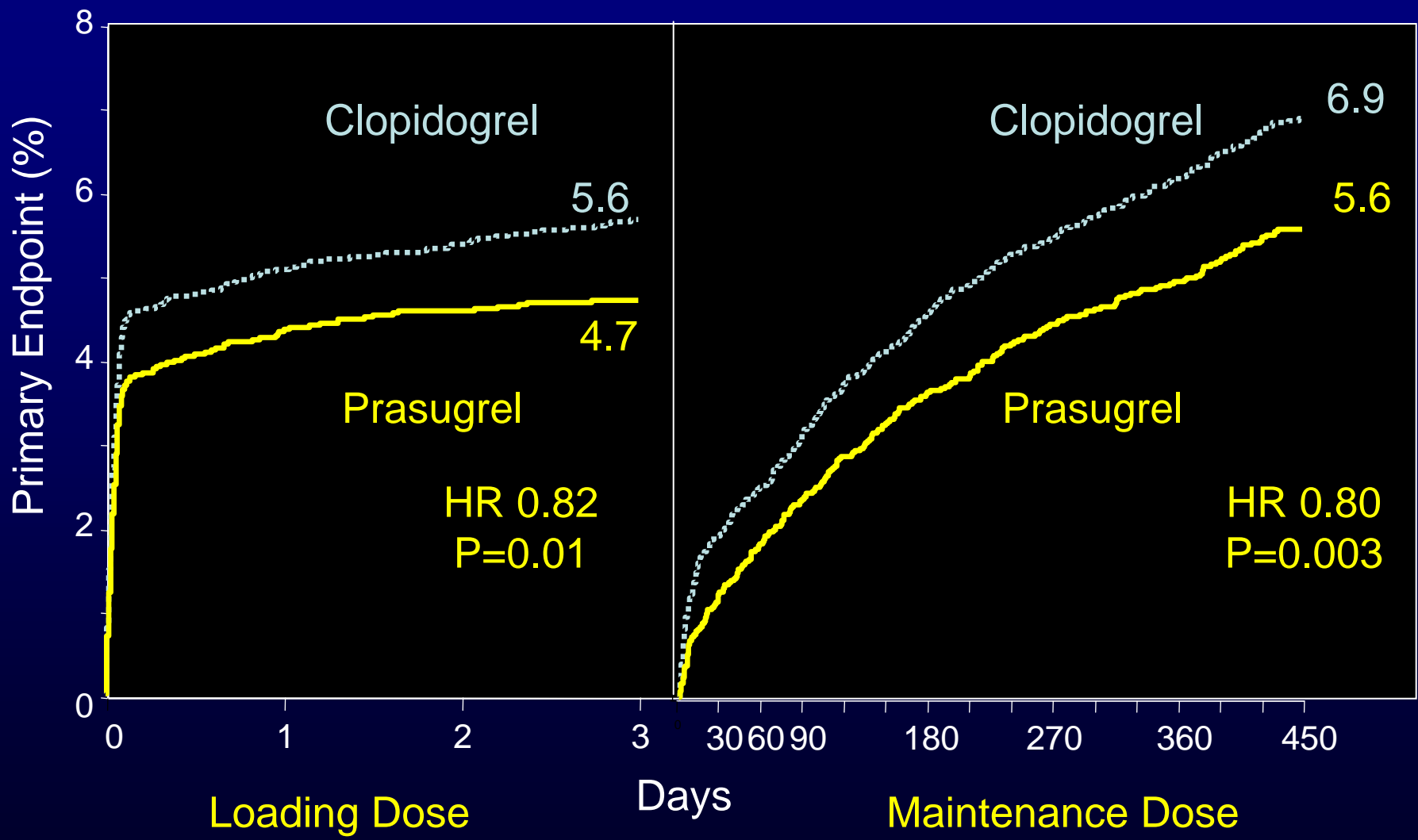
MI Type/Size

Morrow DA, ESC 2008

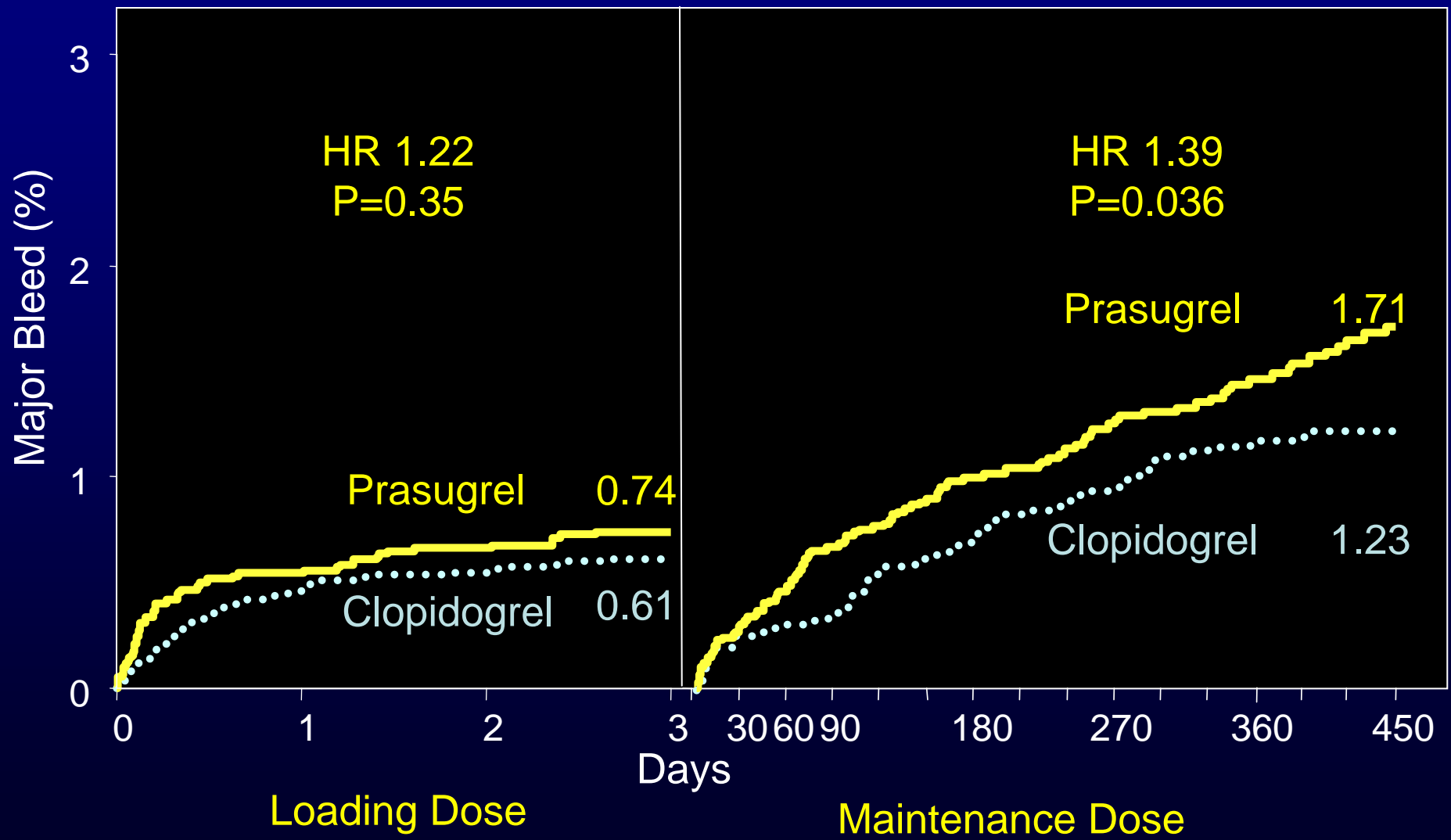
Recurrent Events

Murphy SA, EHJ 2008

Timing of Benefit (Landmark Analysis)

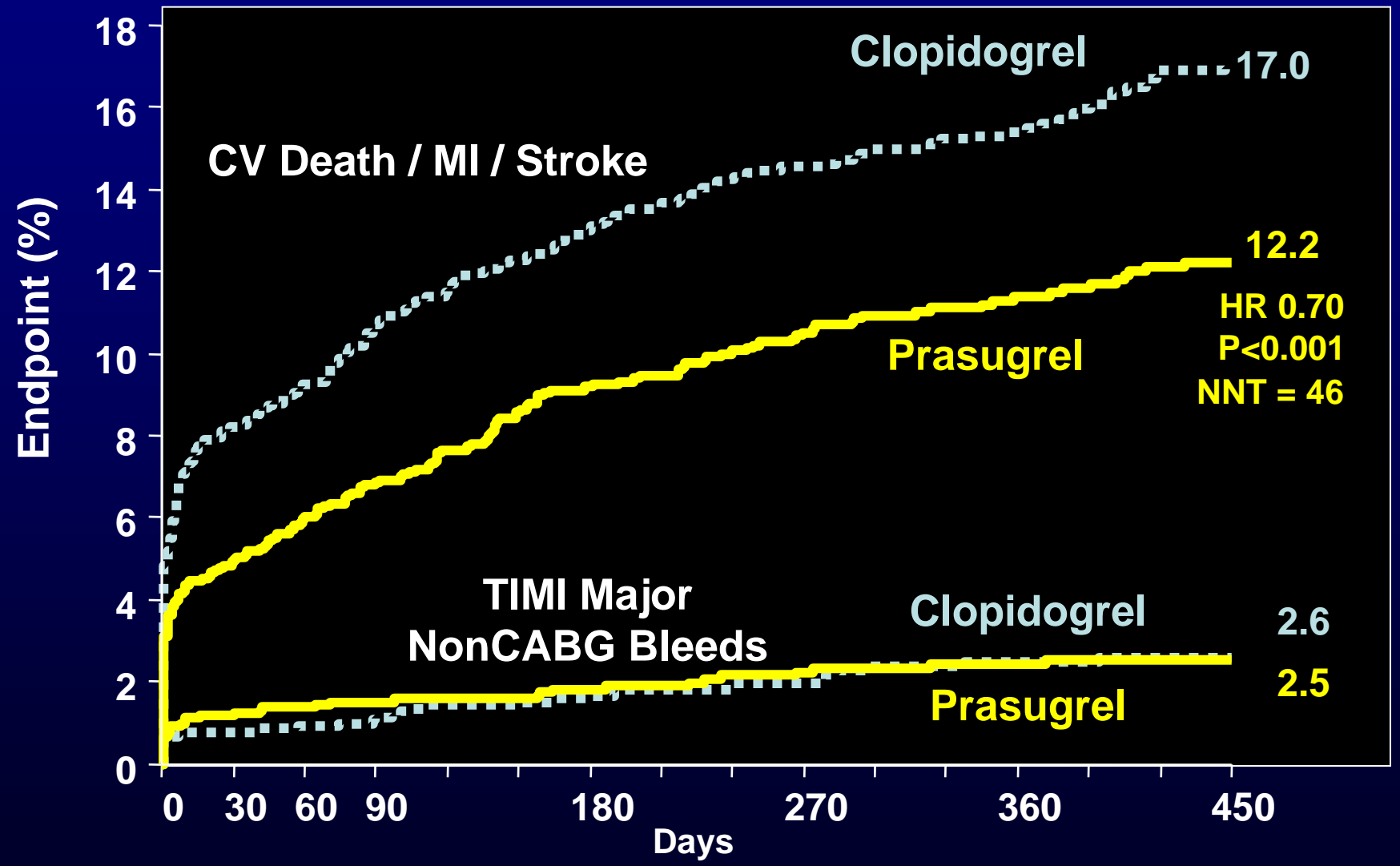


Major Bleed (non CABG) (Landmark Analysis - 3 days)



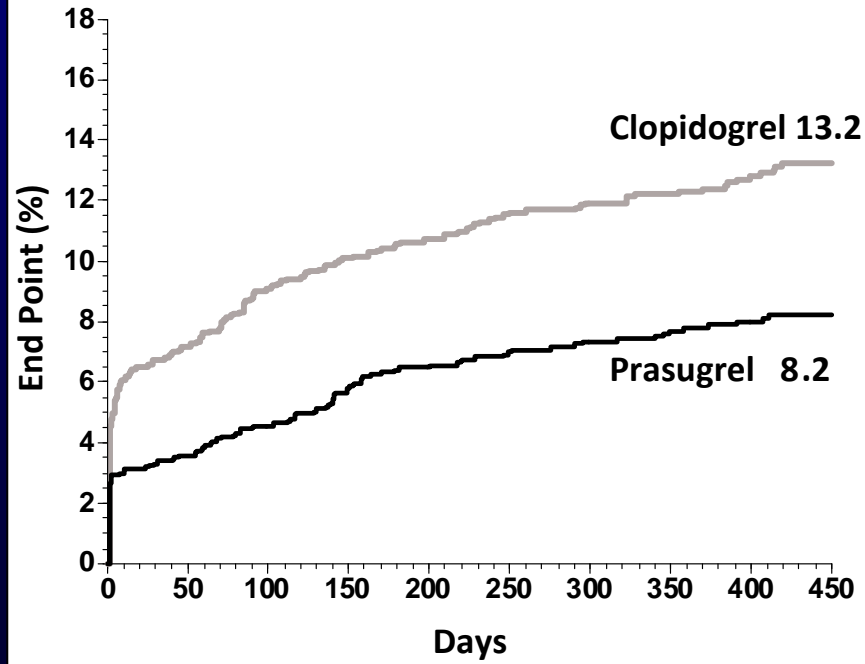
Diabetic Subgroup

N=3146



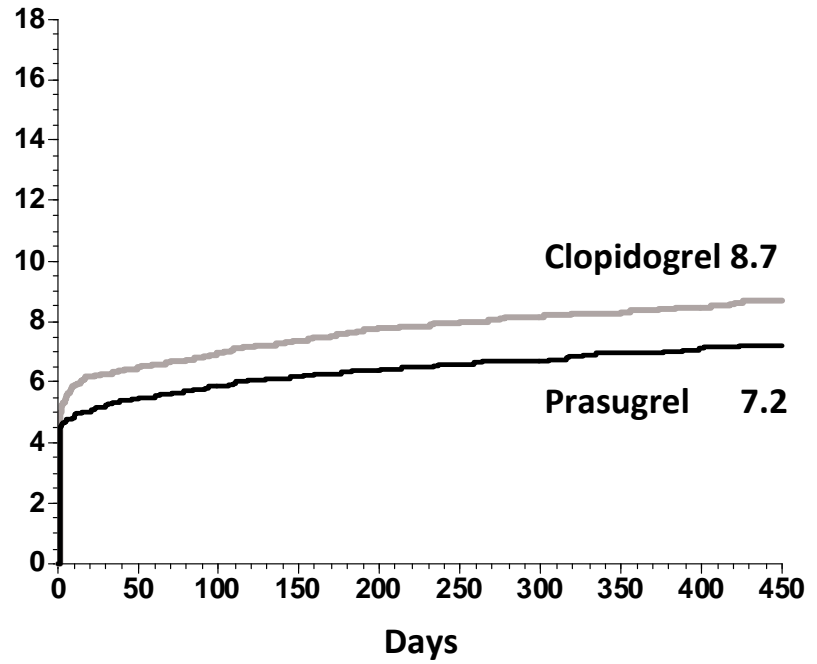
DM

HR 0.60 (0.48-0.76), P<0.001



No DM

HR 0.82 (0.72-0.95), P = 0.006

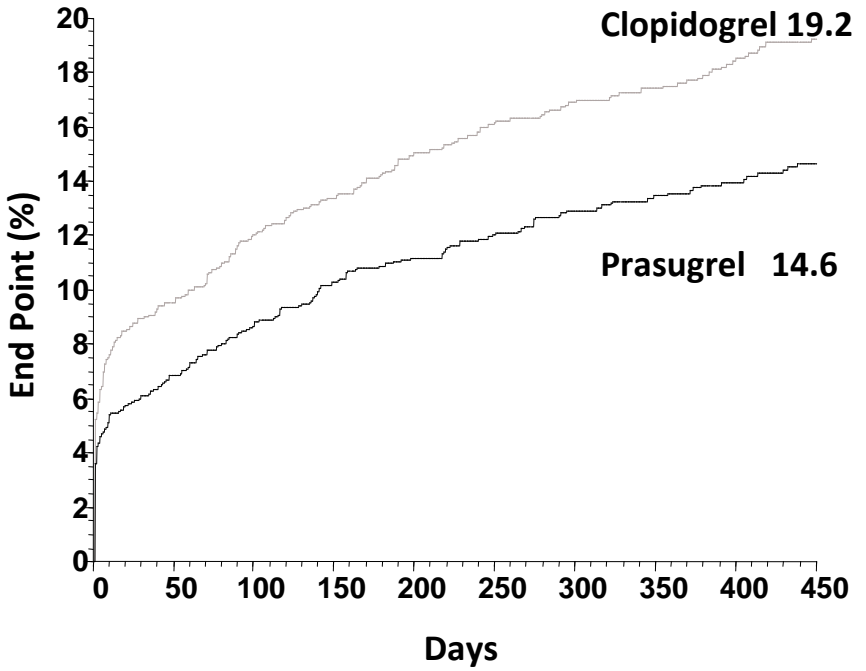


P interaction = 0.02

Net Benefit (D/MI/CVA/Major Bleed)

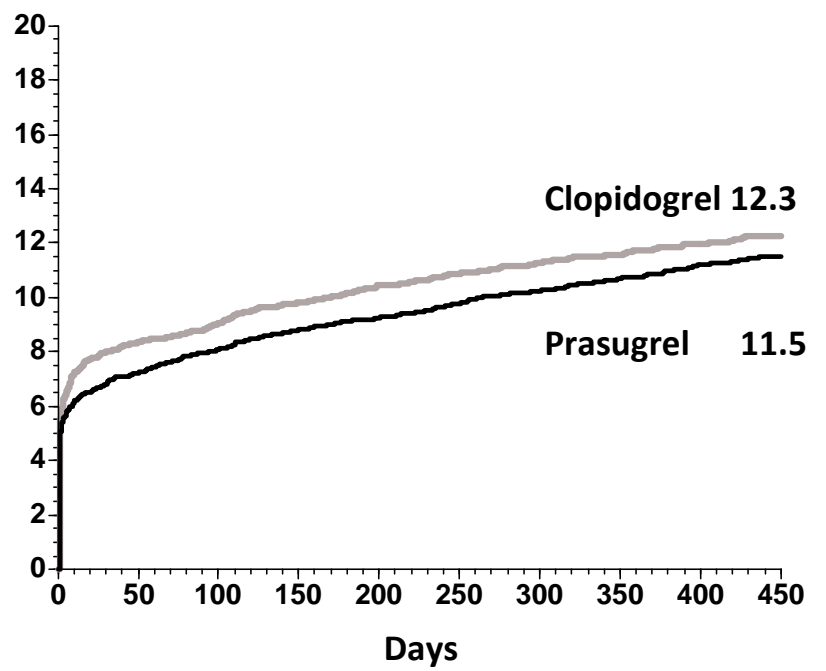
DM

HR 0.74 (0.62-0.89), P = 0.001



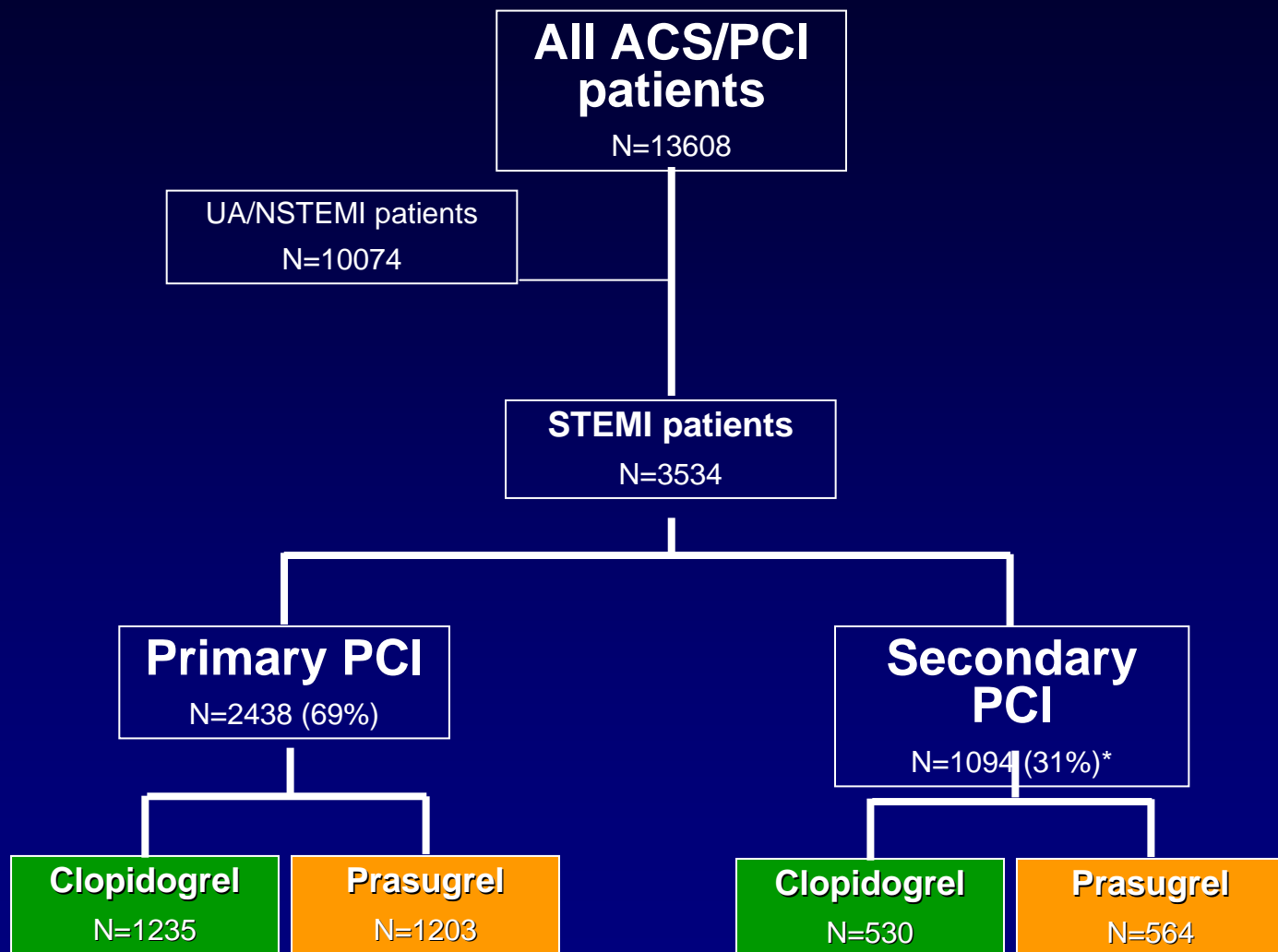
No DM

HR 0.92 (0.82-1.03), P = 0.16



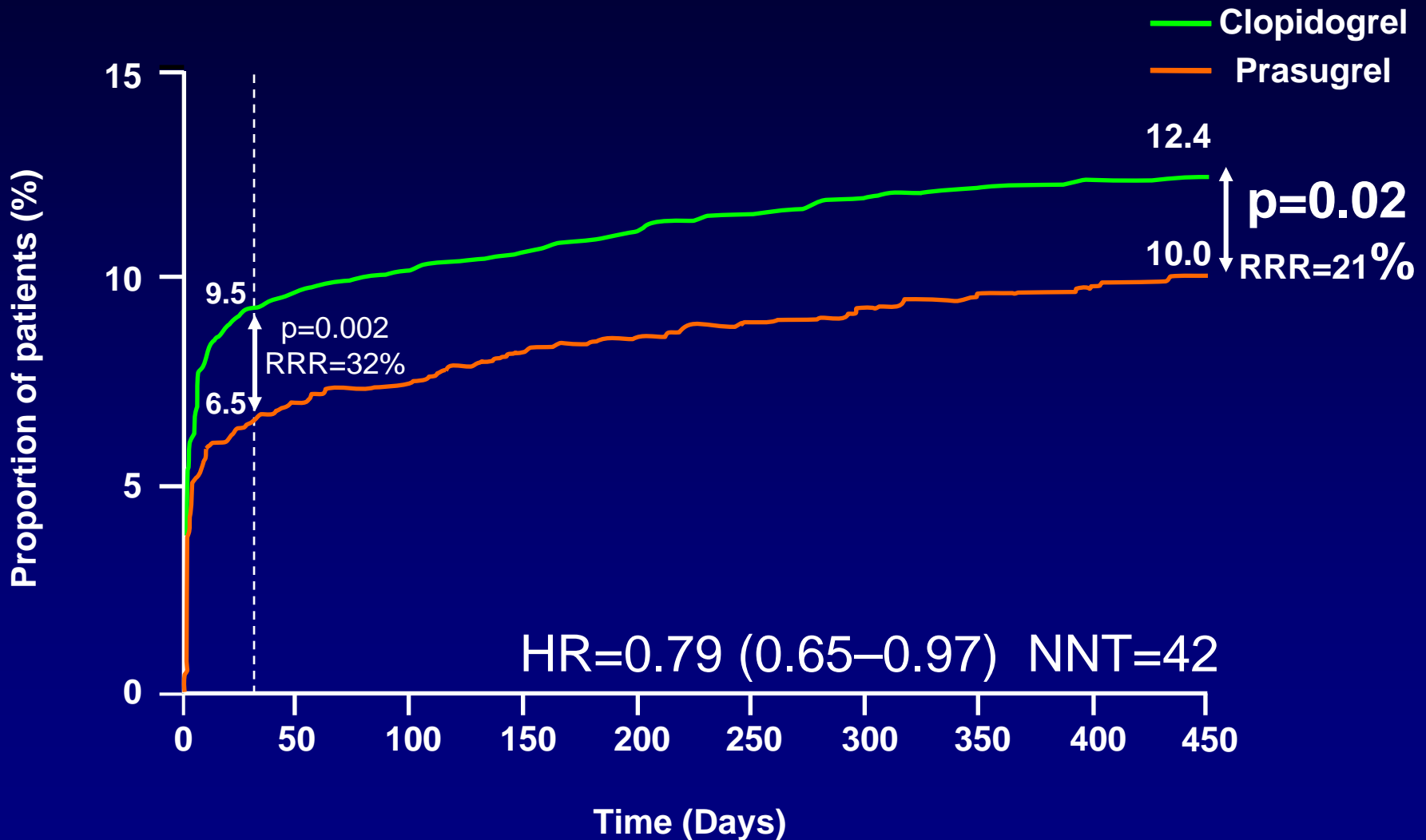
P interaction = 0.05

TRITON-TIMI 38 STEMI

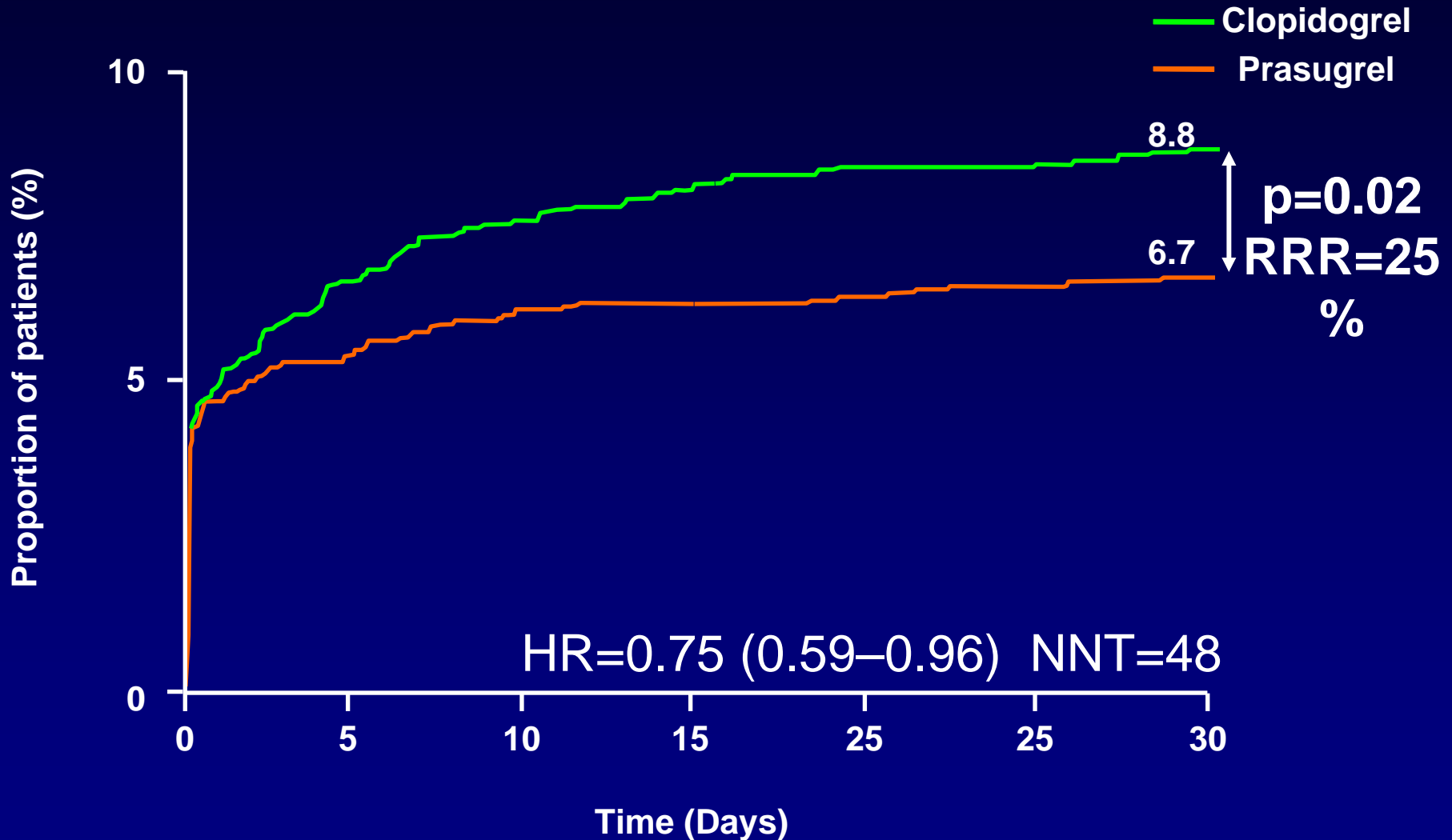


* 2 patients were missing data for primary or secondary

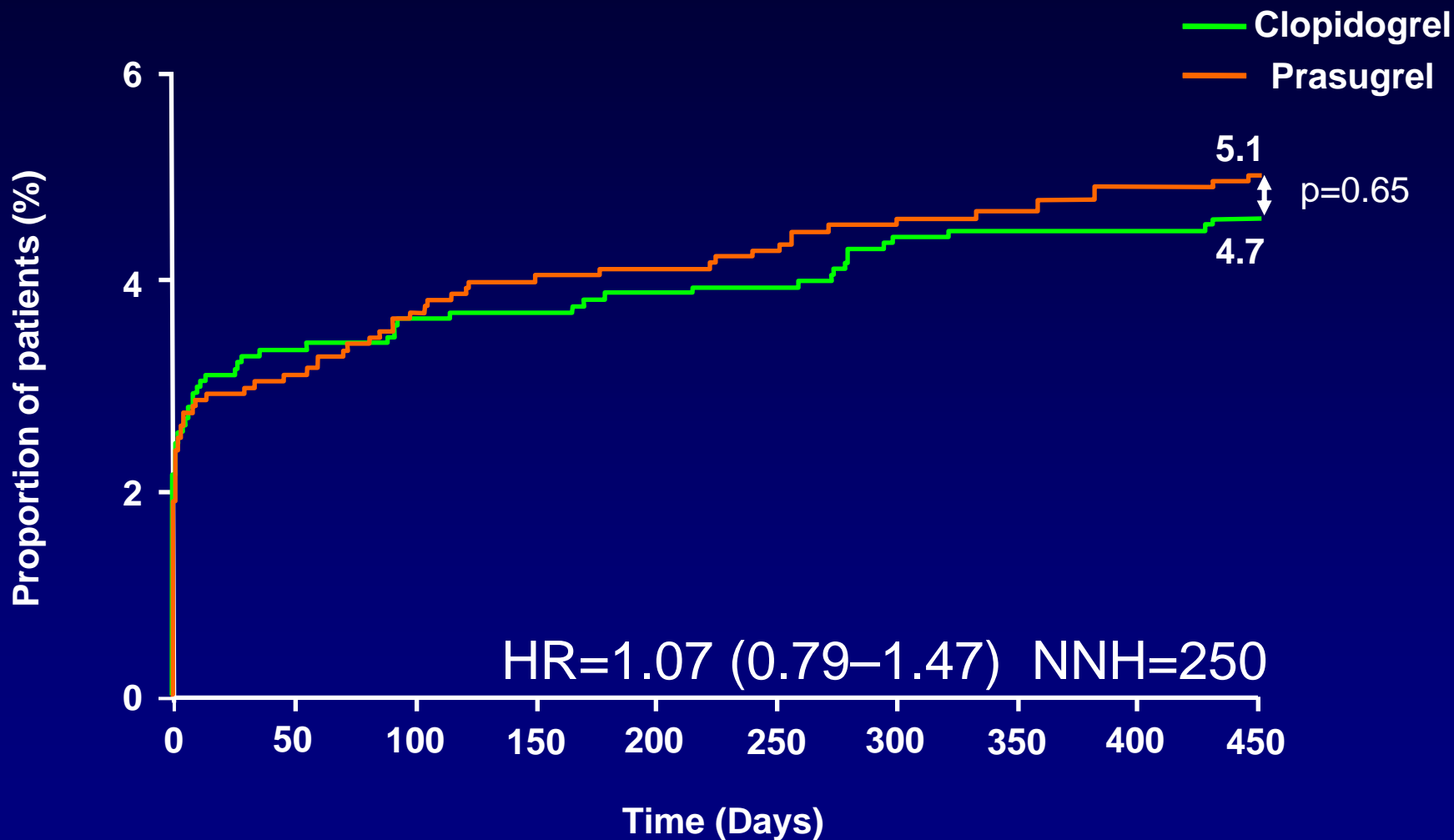
Primary EP (CV death, MI and stroke at 15 months)



Key secondary EP (CV death, MI, and UTVR at 30 days)



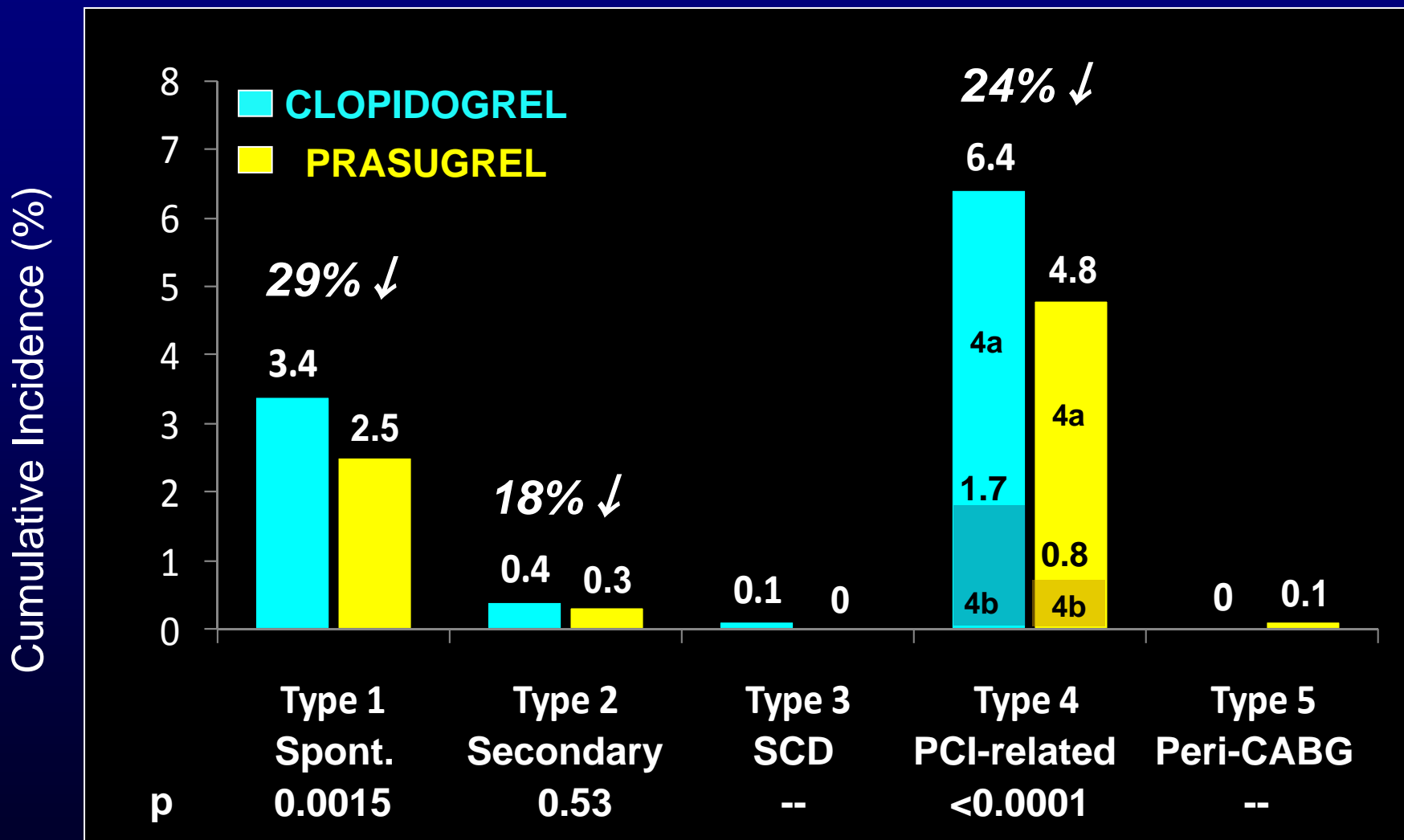
TIMI major or minor non-CABG bleeding



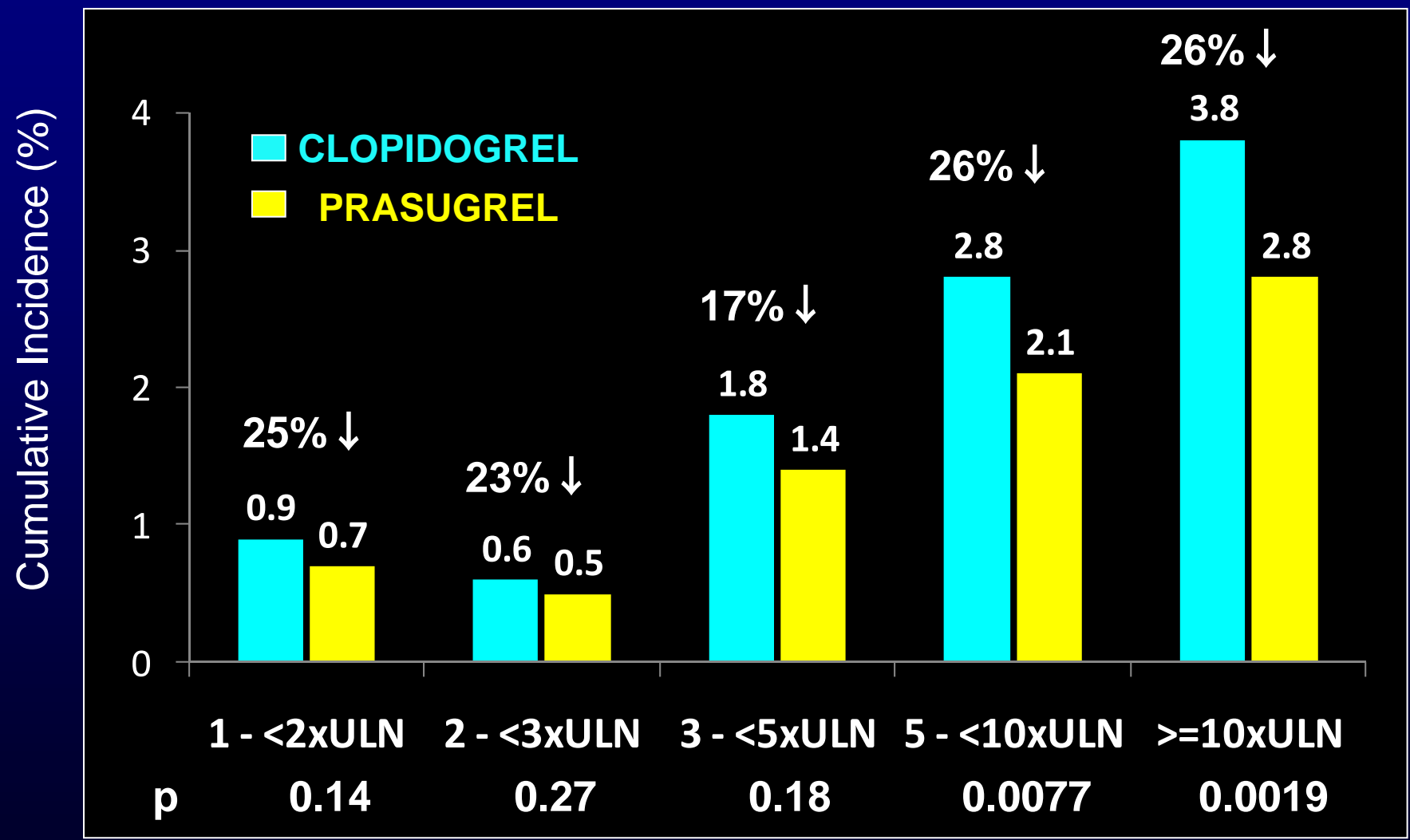
Application of ESC/ACC/AHA/WHF Universal MI Classification

- Supplemental classification of all (total) CEC-adjudicated MI endpoints (N = 1,218)
- Reviewers blinded to treatment allocation.
- Classification by Universal Def. MI Type
 - Type 1: Spontaneous MI
 - Type 2: Secondary MI
 - Type 3: Sudden death due to MI w/out biomarkers
 - Type 4a: Peri-PCI
 - Type 4b: Confirmed stent thrombosis (angio/autopsy)
 - Type 5: Peri-CABG
- Determination of peak CKMB and/or troponin

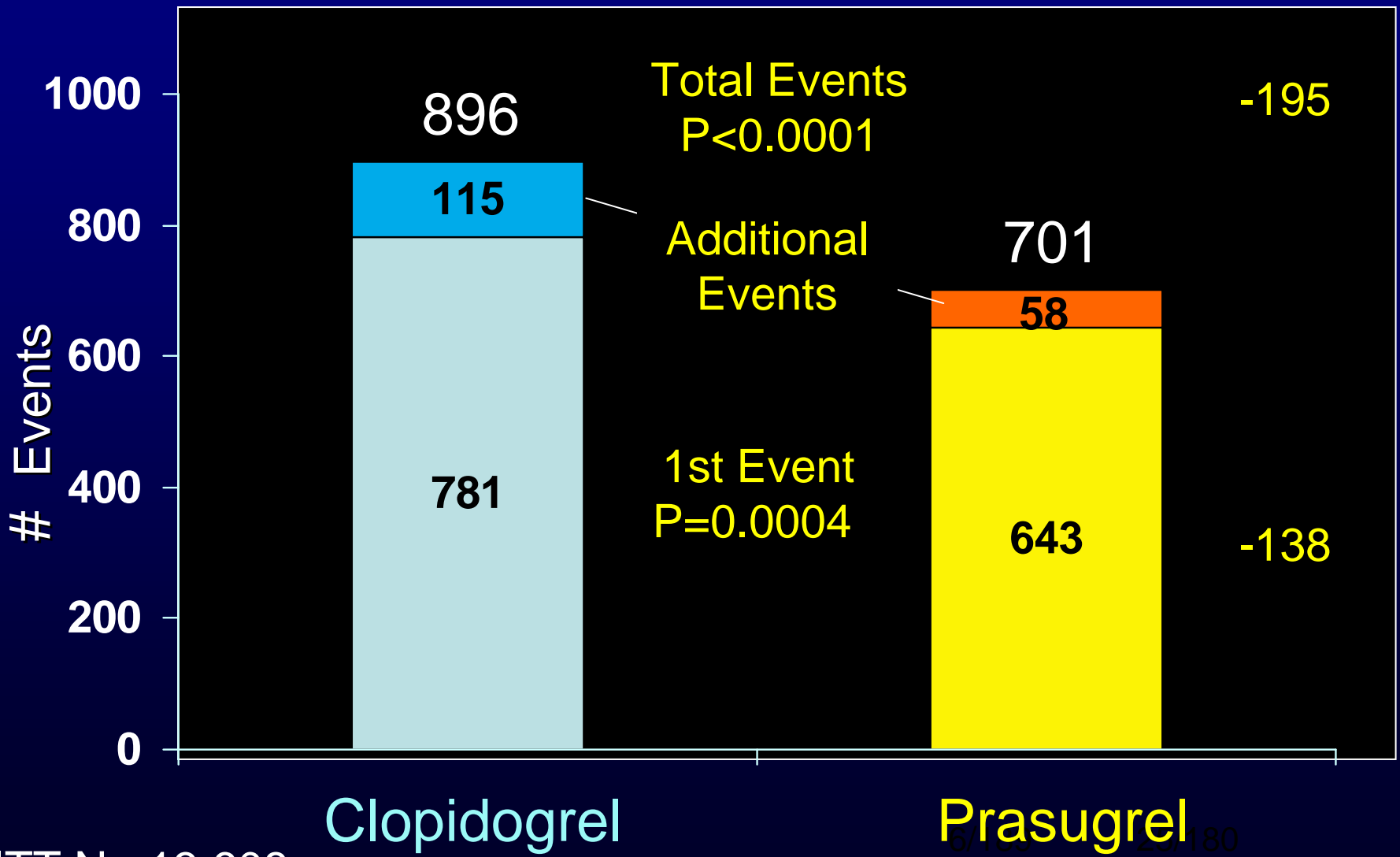
Efficacy Analysis by Universal MI Classification



Efficacy Analysis Peak Biomarker



Total 1^o Endpoint Events Prevented



ITT N= 13,608

What we know now

In ACS patients undergoing PCI:

A thienopyridine agent that achieves faster, more consistent, and greater levels of platelet inhibition ...essentially in a dose response experiment...than standard clopidogrel results in:

- A reduction in ischemic events, particularly myocardial infarction and stent thrombosis
- Higher rates of bleeding, including serious bleeding

What we don't know

What aspect(s) of prasugrel resulted in superiority/risk:

- Speed
- Consistency (fewer poor responders)
- Potency (higher IPA in a population)

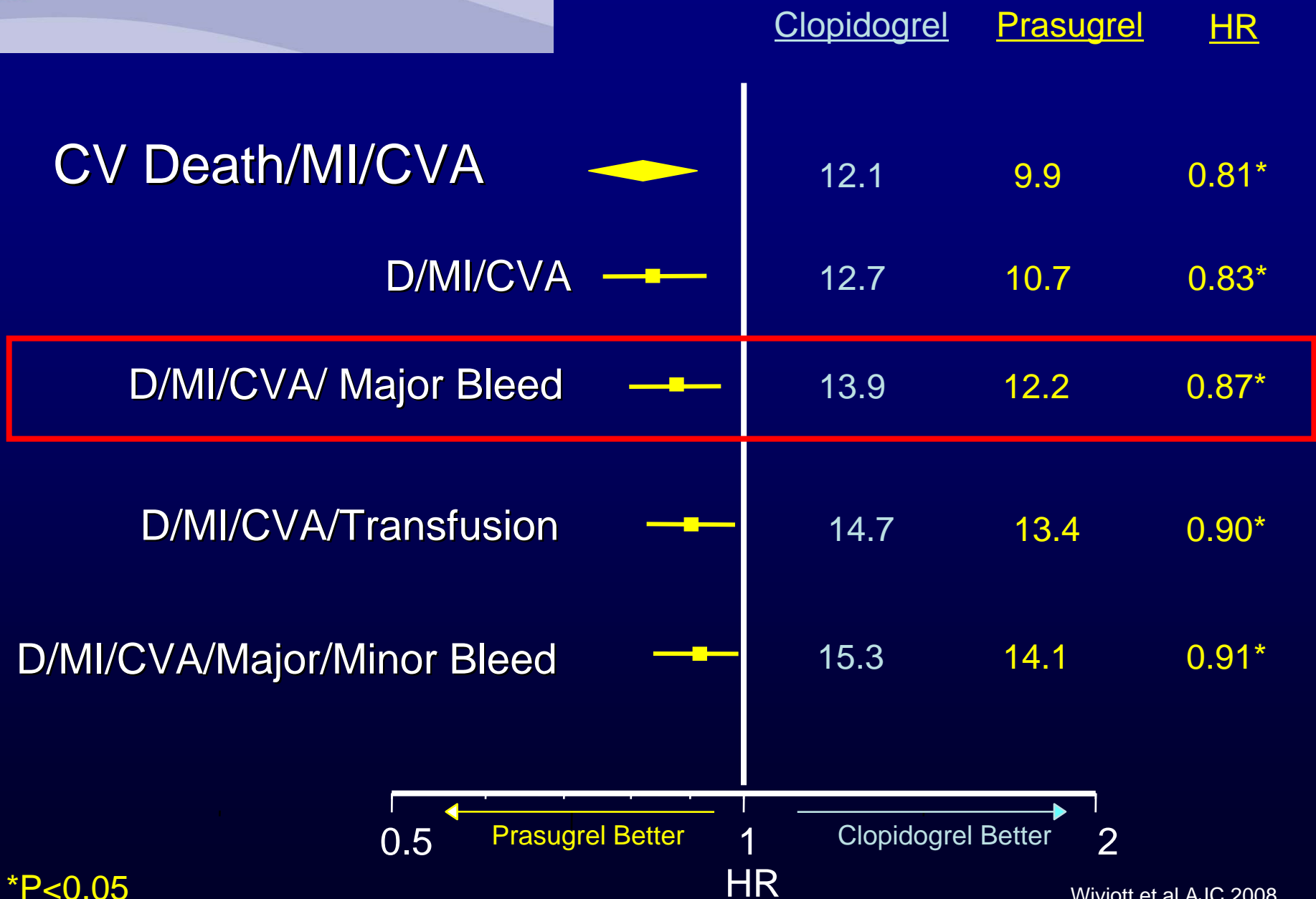
Would this translate to other methods of inhibition of:

- P2Y12 signaling (non-thienopyridine)
- Platelet activation, adhesion, and aggregation unrelated to P2Y12

Can efficacy improvement and bleeding risk be uncoupled for antiplatelet agents?

Are there any appropriate surrogate markers to guide care: IPA, MPA, VASP, POC devices, etc?

Net Benefit Endpoints



*P<0.05