Prasugrel vs. Clopidogrel for Acute Coronary Syndromes Patients Managed without Revascularization — the TRILOGY ACS trial

On behalf of the TRILOGY ACS Investigators

Duke Clinical Research Institute

www.clinicaltrials.gov Identifier: NCT00699998

Committees and Disclosures

Executive Committee

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- Paul Armstrong, MD
- Keith Fox, MB ChB
- Harvey White, MB ChB
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Conflict of Interest Disclosures

- Disclosures for Drs. Roe and Ohman listed on www.dcri.org
- Disclosures for all authors listed within the manuscript

Trial Conduct

- Academic Coordinating Center: DCRI
  - Independently performed statistical analyses
  - Global project management
  - Event adjudication activities
- Global Trial Operations: Quintiles
  - Site management
  - Data management
- Sponsors: Eli Lilly and Daiichi Sankyo
- Protocol Adherence
  - Total of 18 patients lost to follow-up (0.2% of overall)
  - Median study follow-up: 17.1 months (10.4, 24.4)

TRILOGY ACS Study Design

Medically Managed UA/NSTEMI Patients

Randomization Stratified by:
Age, Country, Prior Clopidogrel Treatment
(Primary analysis cohort — Age < 75 years)

N = 9326
< 75 years = 7243
≥ 75 years = 2083

Medical Management Decision ≤72 hrs
(No prior clopidogrel given) — 4% of total

- **Clopidogrel**[1]: 300 mg LD + 75 mg MD
- **Prasugrel**[1]: 30 mg LD + 5 or 10 mg MD

Medical Management Decision ≤ 10 days
(Clopidogrel started ≤ 72 hrs in-hospital OR on chronic clopidogrel) — 96% of total

- **Clopidogrel**[1]: 75 mg MD
- **Prasugrel**[1]: 5 or 10 mg MD

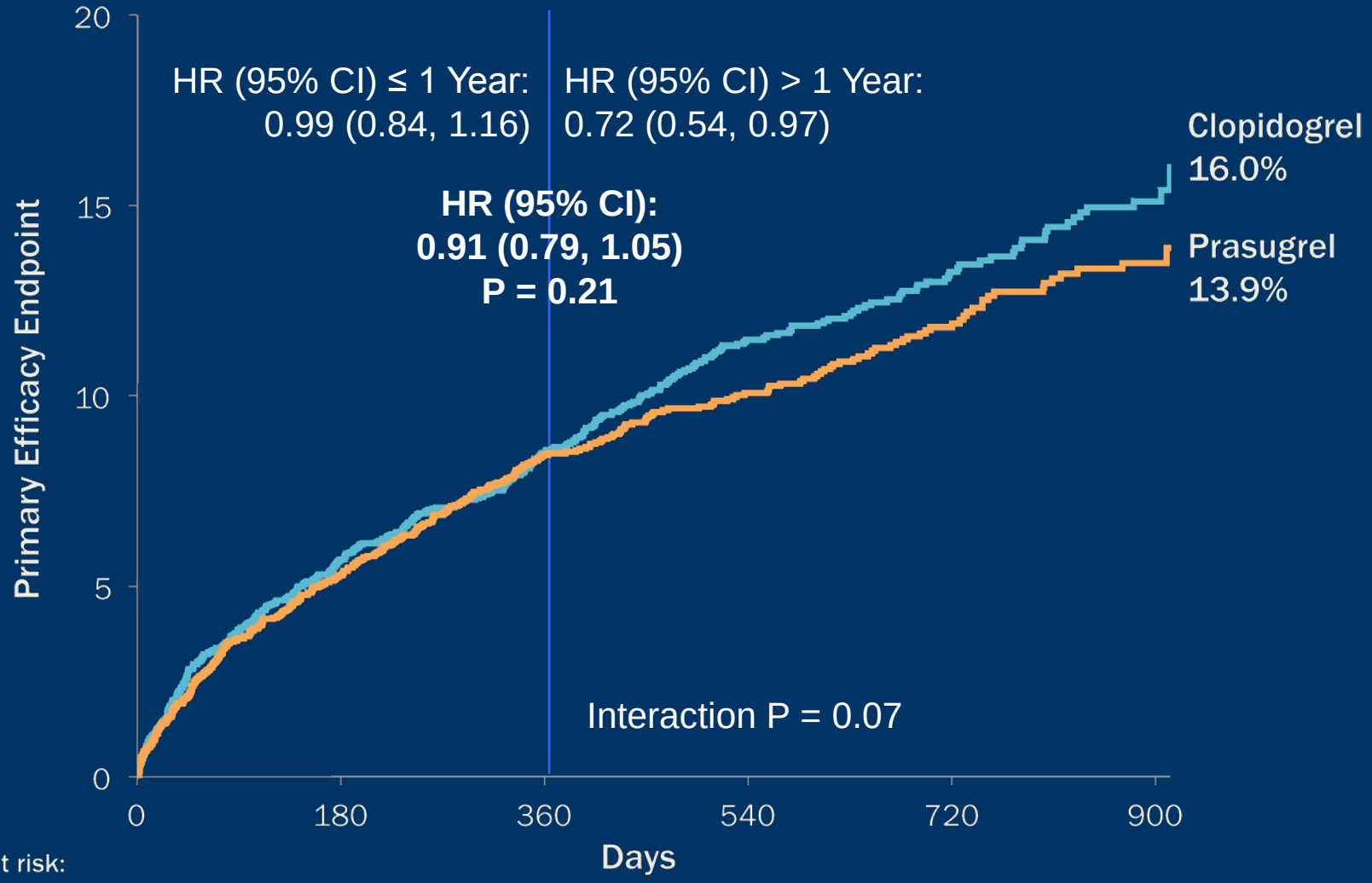
Minimum Rx Duration: 6 months; Maximum Rx Duration: 30 months

Primary Efficacy Endpoint: CV Death, MI, Stroke

1. All patients were on aspirin and low-dose aspirin (< 100 mg) was strongly recommended. For patients <60 kg or ≥75 years, 5 mg MD of prasugrel was given. Adapted from Chin CT et al. *Am Heart J* 2010;160:16-22.e1.

Primary Efficacy Endpoint to 30 Months

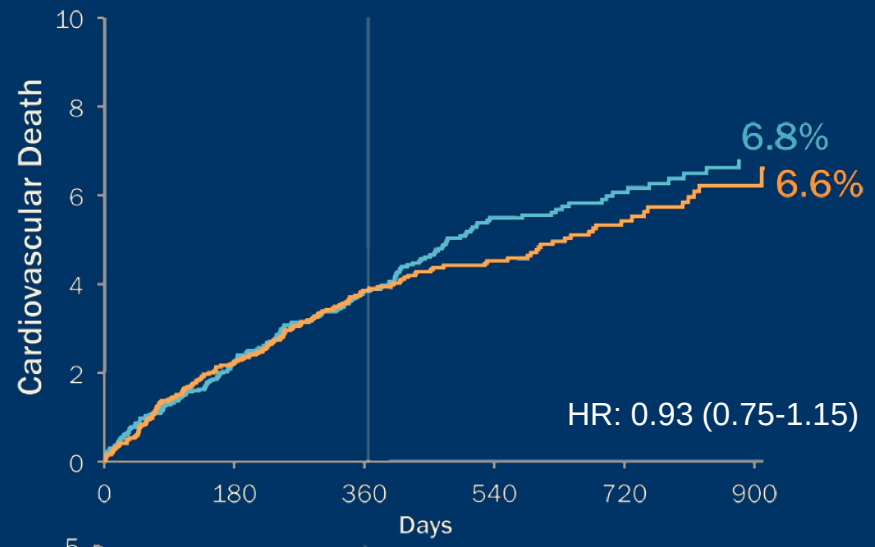
(Age < 75 years)

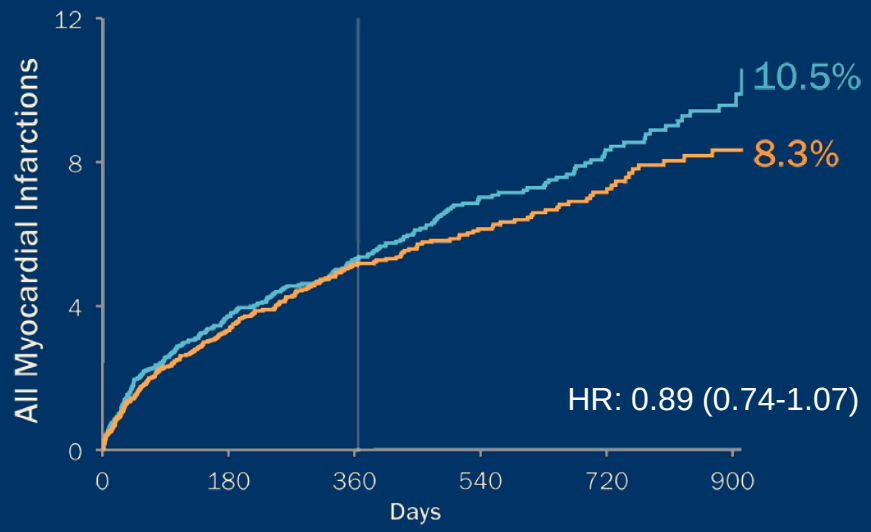


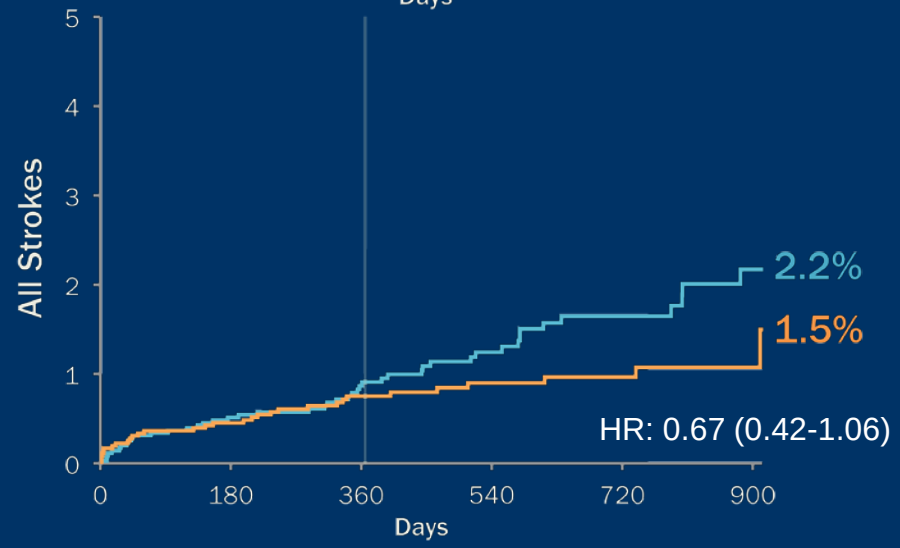
No. at risk:

Prasugrel:	3620	3248	2359	1611	953	389
Clopidogrel:	3623	3244	2390	1596	946	399

Efficacy Component Endpoints to 30 Months
(Age < 75 years)







	HR (95% CI) ≤ 1 Year	HR (95% CI) > 1 Year
CV Death	1.00 (0.78, 1.28)	0.75 (0.49, 1.14)
All MI	0.97 (0.78, 1.19)	0.68 (0.46, 0.99)
All Stroke	0.86 (0.50, 1.47)	0.35 (0.14, 0.88)

Evaluation of All Ischemic Events Over Time*

(Age < 75 years)

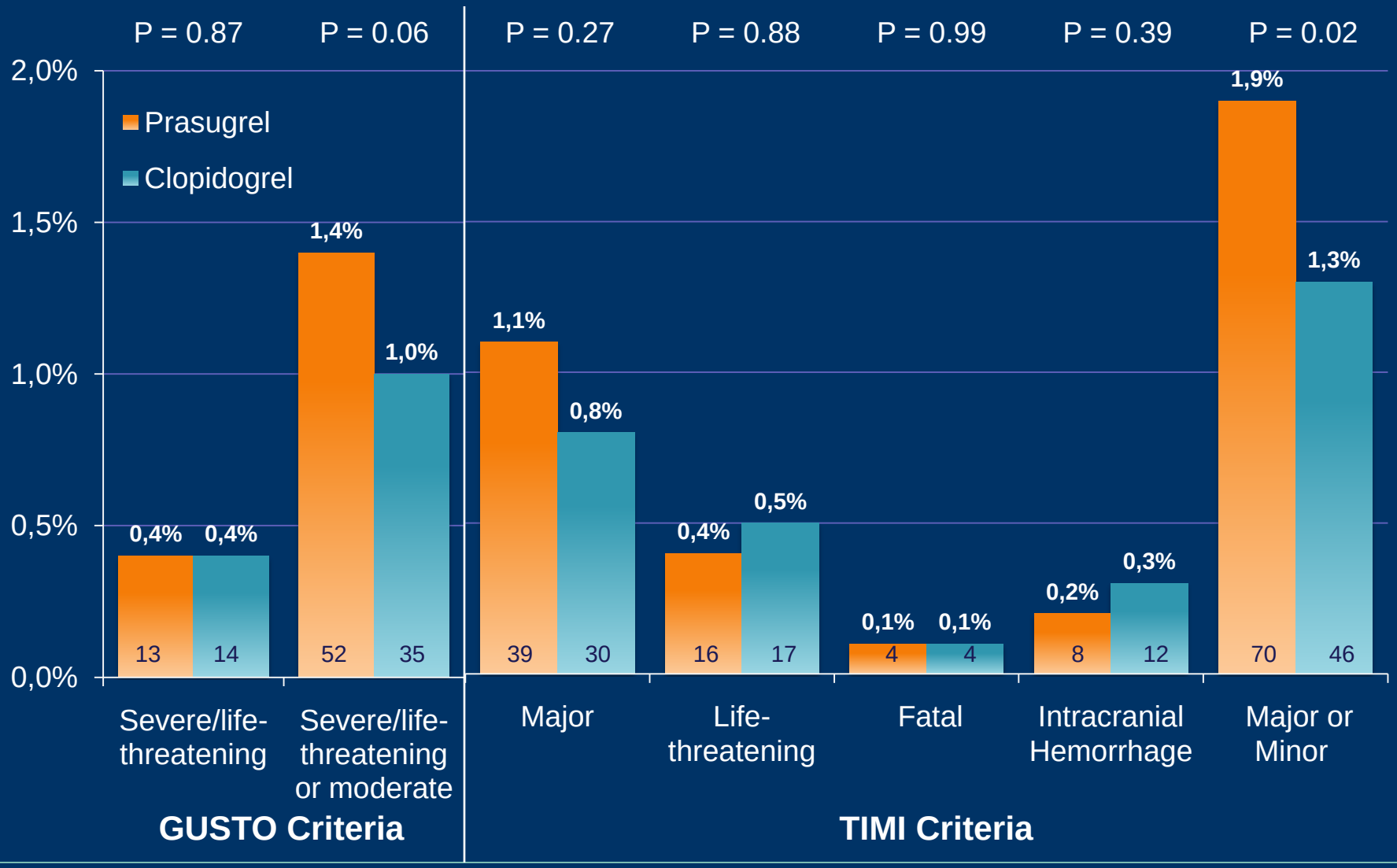
- Lower risk multiple recurrent ischemic events suggested with prasugrel using the pre-specified Andersen-Gill model (HR = 0.85, 95% CI: 0.72–1.00, P=0.04)
- Significant interaction with treatment and time (HR for > 12 mos = 0.64, 95% CI: 0.48–0.86, Interaction P=0.02)

	Prasugrel	Clopidogrel
≥ 1 event	364	397
≥ 2 events	77	109
3–7 events	18	24

* Pre-specified evaluation of all CV death, MI, or stroke events by treatment

Incidence of Bleeding Outcomes

(Age < 75 years)



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Incidence of Key Safety Outcomes
(Overall Population)

	Prasugrel	Clopidogrel	Hazard Ratio (95% CI)	P Value
Bleeding	(N = 4623)	(N = 4617)		
GUSTO Severe/life-threatening bleeding	22 (0.5%)	27 (0.6%)	0.83 (0.48–1.46)	0.53
TIMI Fatal Bleeding	7 (0.2%)	9 (0.2%)	0.80 (0.30–2.14)	0.68
Intracranial Hemorrhage	14 (0.3%)	19 (0.4%)	0.76 (0.38–1.51)	0.42
Neoplasm				
New, non-benign neoplasms*	82 (1.8%)	78 (1.7%)	1.05 (0.77-1.43)	0.79
Mortality	(N = 4663)	(N = 4663)		
All-cause death	385 (8.3%)	409 (8.8%)	0.94 (0.82–1.08)	0.40

*Among patients with no prior history of malignancy or prior malignancy treated with curative therapy

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Conclusions

- In the largest trial to date of ACS patients managed medically without revascularization, prasugrel was not statistically different from clopidogrel during 2.5 years of follow-up among patients < 75 years of age
- Further analyses of the primary endpoint yielded several important findings favoring prasugrel treatment
  - Trend for a time-dependent benefit after 1 year
  - Fewer total recurrent ischemic events, particularly after 1 year
- No statistical difference in major, life-threatening, or fatal bleeding, and no difference in new non-benign neoplasms were observed with prasugrel vs. clopidogrel

ORIGINAL ARTICLE

Prasugrel versus Clopidogrel for Acute Coronary Syndromes without Revascularization

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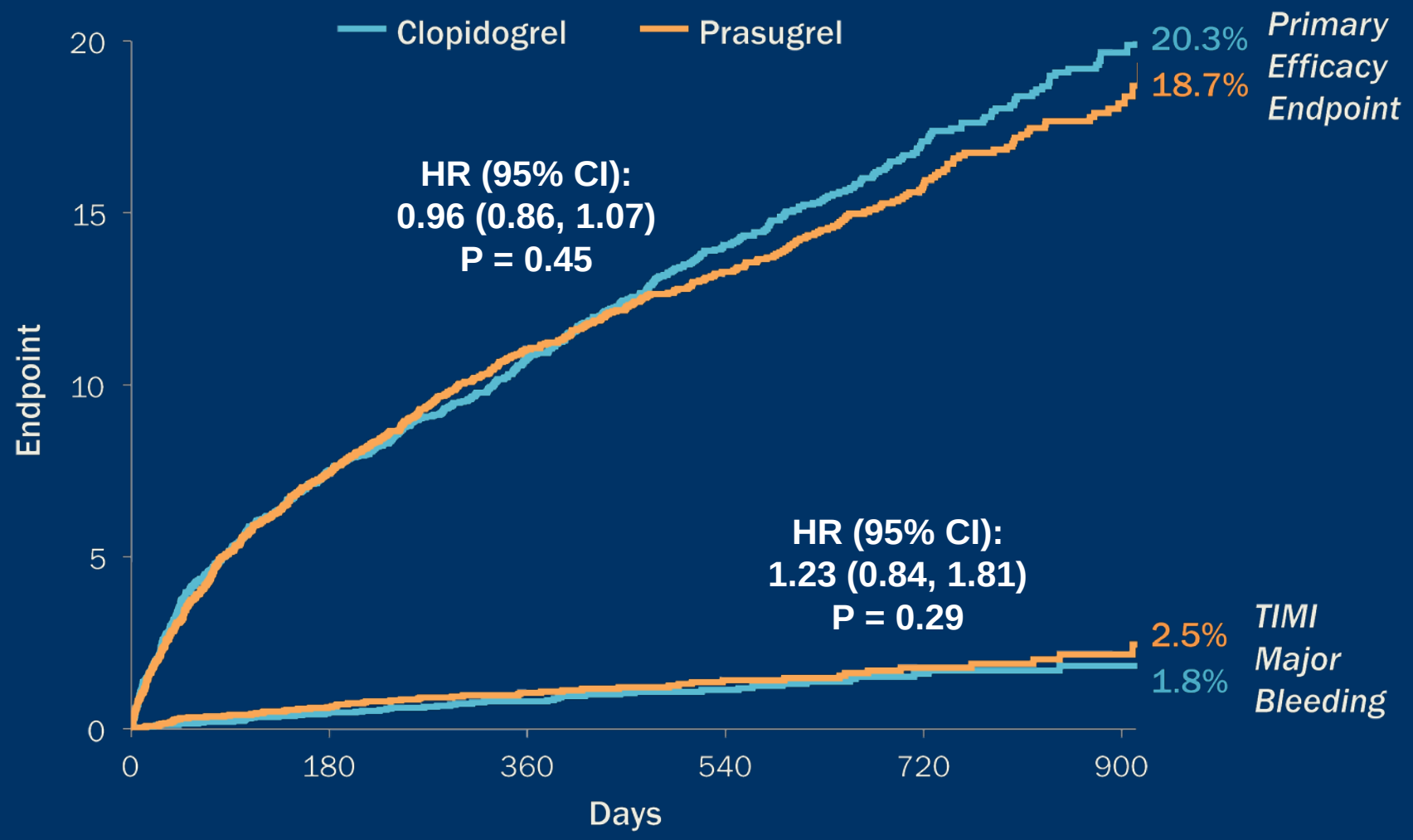
Primary Efficacy Endpoint and TIMI Major Bleeding Through 30 Months

(Overall population)