

# CHAMPION PLATFORM

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Robert A. Harrington, MD, on behalf of the CHAMPION PLATFORM Investigators

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Dr. Bhatt has received (significant) institutional research support from: Astra Zeneca, Bristol-Myers Squibb, Eisai, Ethicon, Heartscap, sanofi aventis, The Medicines Company.

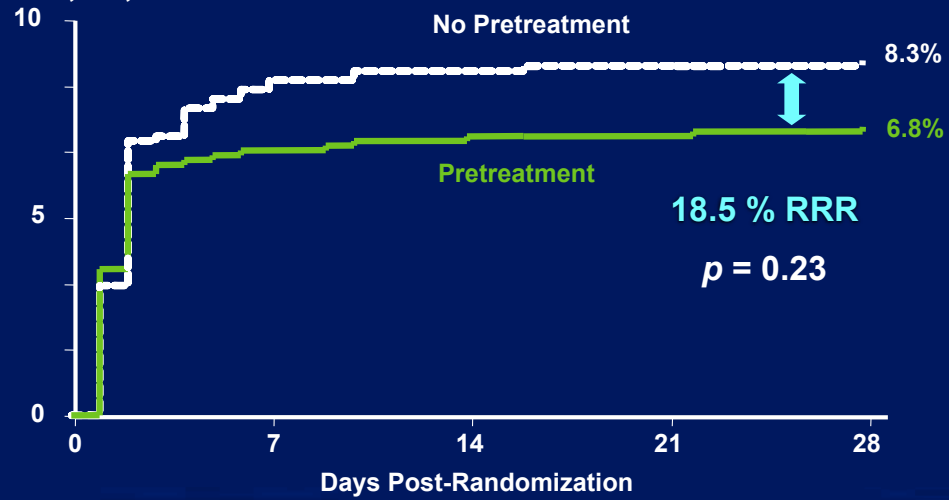
This presentation includes off label and/or investigational uses of drugs.

- Observational and subgroup analyses have shown that pretreatment with oral ADP receptor blockers prior to PCI reduces ischemic events
- If there is a need for emergent CABG, however, bleeding is increased with currently available oral agents
- Furthermore, it is not clear what the optimal timing of pretreatment with oral agents may be around the time of PCI

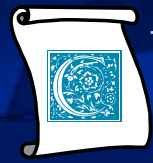


# CREDO: 28-Day Endpoint

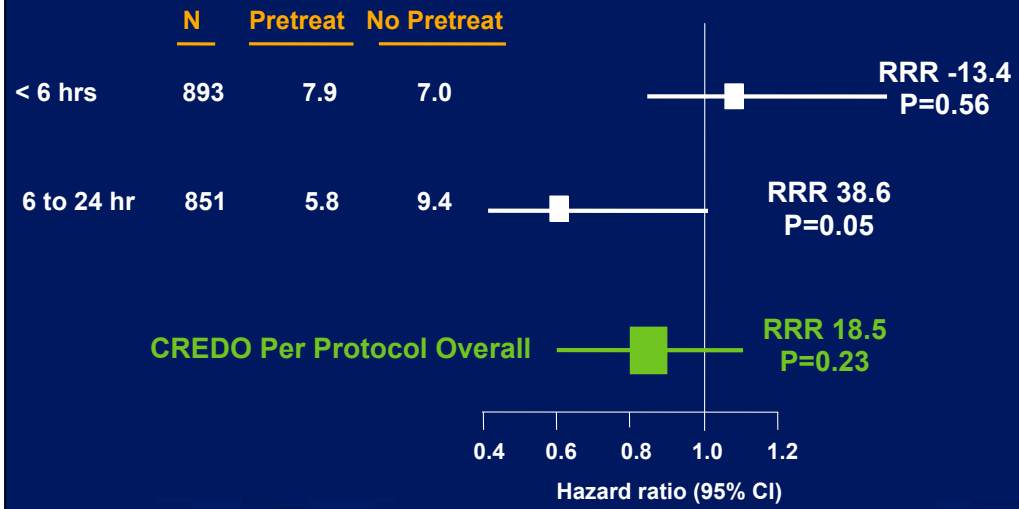
Death, MI, or UTVR



Steinhubl SR, et al. *JAMA* 2002; 288:2411-20.



# Timing of Loading Dose and 28-Day Endpoint



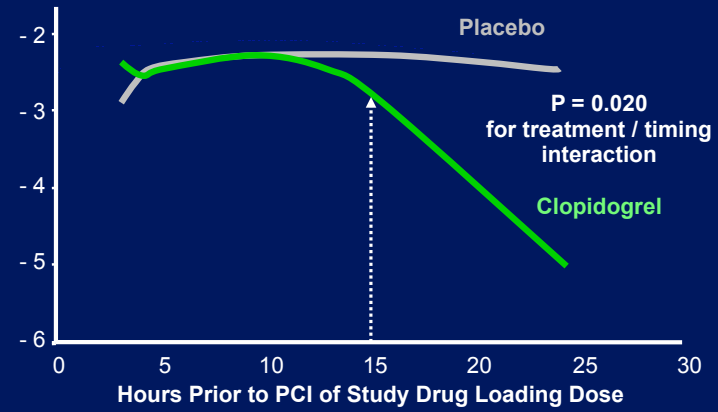
Steinhubl SR, et al *JAMA* 2002; 288:2411-20.



# CREDO: Clopidogrel Loading Dose Timing vs Risk of MACE



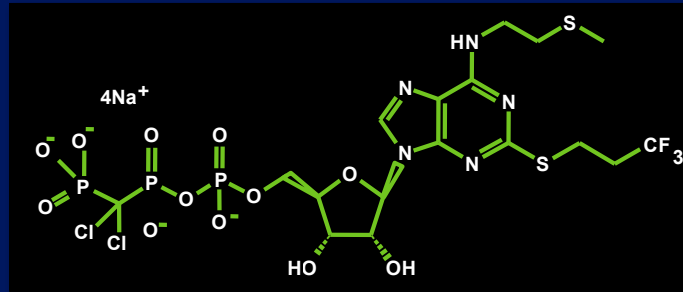
Log Odds of Death, MI  
or UTVR at 28 Days



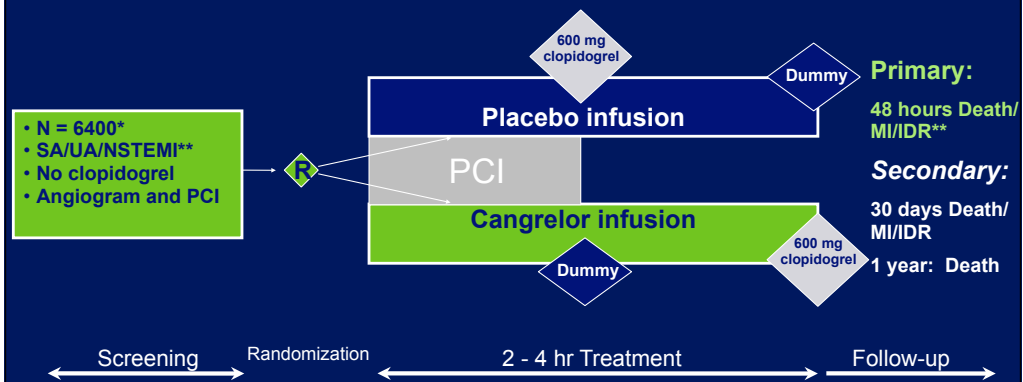
Steinhubl SR, et al. *JACC* 2006;47:939-43.

## Intravenous ADP-P2Y<sub>12</sub> receptor antagonist

- Rapid acting: quick onset, quick offset
- Plasma half-life of 3 – 6 minutes
- 60 minutes for return to normal platelet function



# PLATFORM: Study Design



\* Study stopped by IARC, ITT population = 5362

\*\*SA= stable angina, UA= unstable angina, NSTEMI= non-ST segment elevation myocardial infarction, MI= myocardial infarction, IDR= ischemic-driven revascularization

- Death - All cause mortality
- Myocardial Infarction (MI)
  - Data collection
    - 1 baseline, sampling at 2h, 10h, 18h, 24h
      - Baseline: troponin and CKMB
      - Post-baseline: CKMB; troponin if available
  - CEC adjudication
    - Followed generally accepted criteria for post-PCI MI in 2006
      - 3X ULN
      - Required 50% increase if baseline CKMB/troponin positive
      - CKMB primary marker
    - CEC “rule” to exclude elevations < 6 hrs post randomization

- Myocardial Infarction (MI) Continued
  - Q-wave-MI
    - New Q waves w/duration of > 0.03 sec in 2 contiguous leads
    - CEC adjudicated
- Ischemia Driven Revascularization (IDR)
  - Requires clinical signs or ST changes
  - Within 24 hours
- Definite Stent Thrombosis
  - Adjudicated as part of IDR
  - Angiographically documented re-study for documented ischemia
    - Acute: Within 24 hours
    - Subacute: Between 24 hours and 30 days

| PLATFORM                              |                       |
|---------------------------------------|-----------------------|
| Initial Sample Size                   | 6400 modified ITT     |
| Estimated event rate clopidogrel arm  | 7.7%                  |
| Estimated effect size                 | 25%                   |
| Power                                 | 85%                   |
| Final enrollment (as of May 13, 2009) | 5362 (84% of planned) |

# CHAMPION PLATFORM Top 10 Enrollers



| Country        | PI          | Hospital  | Enrollment |
|----------------|-------------|---|------------|
| Bulgaria       | Manukov     | Clinic of Invasive Cardiology, UMHAT "Sveti Georgi" EAD - Plovdiv | 628        |
| Czech Republic | Tousek      | Hospital Ceske Budejovice, Cardiocenter - cardiology              | 417        |
| USA            | McLaurin    | Anderson Area Medical Center                                      | 170        |
| India          | Arneja      | Arneja Heart Institute  | 127        |
| USA            | Jafar       | Hudson Valley Heart Center/Vassar Brothers Medical Center         | 123        |
| India          | Banker      | Bankers Heart Institute   | 103        |
| India          | Patel       | Krishna Heart and Super Speciality Institute                      | 91         |
| USA            | Smith       | Trinity Mother Francis Hospital, East Texas Med Center            | 68         |
| USA            | Scott       | University of Tennessee Medical Center                            | 67         |
| Thailand       | Kuanprasert | Maharaj Nakorn Chiang Mai Hospital                                | 66         |

## Demographics and History



| Characteristic   | Cangrelor<br>N= 2693 | Comparator<br>N=2669 |
|------------------|----------------------|----------------------|
| Age, yrs (IQR)   | 63.0 (54.0, 71.0)    | 63.0 (54.0, 71.0)    |
| Female           | 28.0%                | 29.7%                |
| Weight , kg      | 80.0 (70.0, 92.0)    | 80.0 (70.0, 92.0)    |
| Smoker           | 31.8%                | 30.4%                |
| Diabetes         | 30.8%                | 32.6%                |
| Prior MI         | 24.1%                | 25.7%                |
| Prior PCI        | 14.2%                | 15.5%                |
| Hypertension     | 74.3%                | 74.5%                |
| Hyperlipidemia   | 53.5%                | 54.0%                |
| Hx of CAD        | 36.4%                | 36.0%                |
| Prior stroke/TIA | 6.0%                 | 6.0%                 |

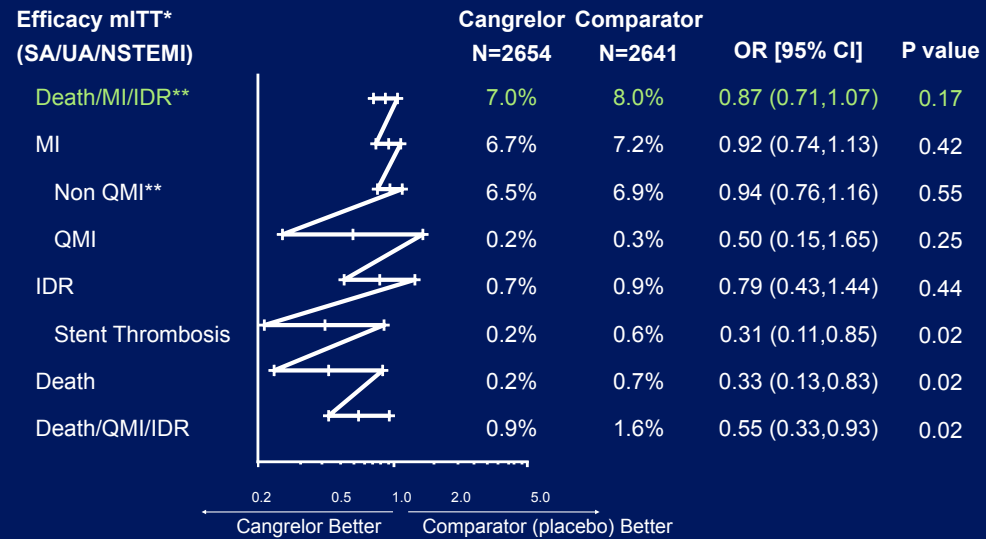
| Characteristic                            | Cangrelor<br>N= 2693 | Comparator<br>N=2669 |
|---|----------------------|----------------------|
| Stable angina                             | 5.4%                 | 5.3%                 |
| Unstable angina                           | 35.2%                | 34.4%                |
| Non-ST-segment elevation MI               | 59.4%                | 60.3%                |
| Hospital Admission to Angiography, median | 6.1 h                | 6.4 h                |
| Hospital admission to randomization       | 7.5 h                | 7.8 h                |
| Hospital Admission to PCI, hours, median  | 7.8 h                | 8.1 h                |

# Presentation and Procedural Characteristics



| Characteristic              | Cangrelor<br>N= 2693 | Comparator<br>N=2669 |
|-----------------------------|----------------------|----------------------|
| Number of target vessels:   |                      |                      |
| 1                           | 83.5%                | 83.2%                |
| 2                           | 15.5%                | 15.5%                |
| 3                           | 0.7%                 | 1.1%                 |
| DES used                    | 38.9%                | 38.6%                |
| Non-DES                     | 56.8%                | 57.1%                |
| Duration infusion, median h | 2.1 (2.0, 2.3)       | 2.1 (2.0, 2.3)       |

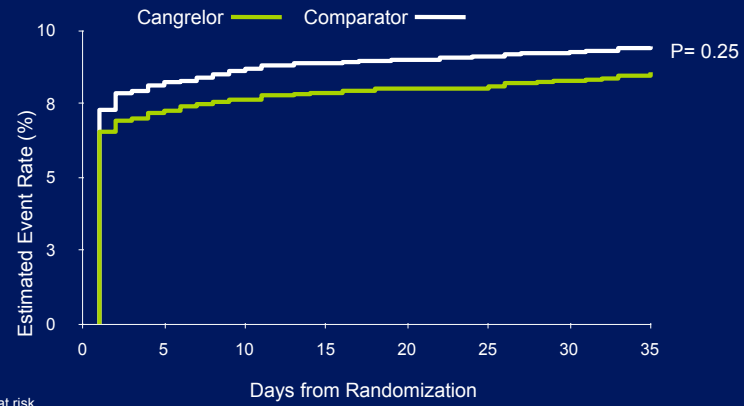
# Efficacy Endpoints at 48 Hours



\* \*Primary Analysis

\*\* mITT= modified intent to treat population (patients with PCI and study drug), QMI= Q-wave myocardial infarction

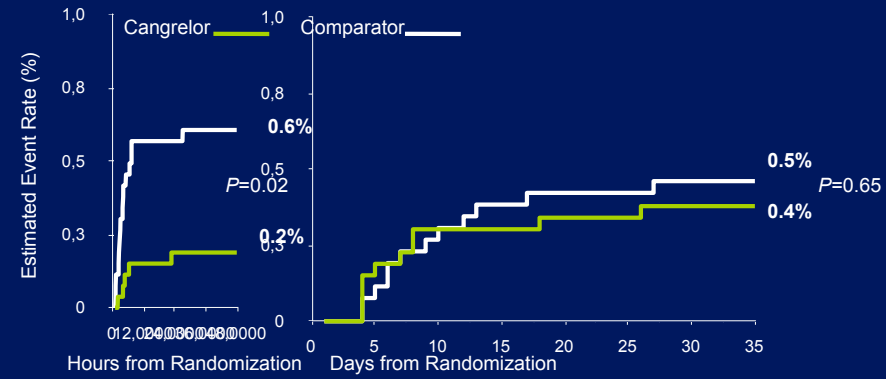
# 30-Day Time-to-Event Analysis Endpoint: Death/MI/IDR



Patients at risk

|            | 0    | 5    | 10   | 15   | 20   | 25   | 30   | 35   |
|------------|------|------|------|------|------|------|------|------|
| Cangrelor  | 2656 | 2461 | 2448 | 2441 | 2437 | 2437 | 2425 | 1557 |
| Comparator | 2645 | 2427 | 2409 | 2402 | 2399 | 2396 | 2389 | 1552 |

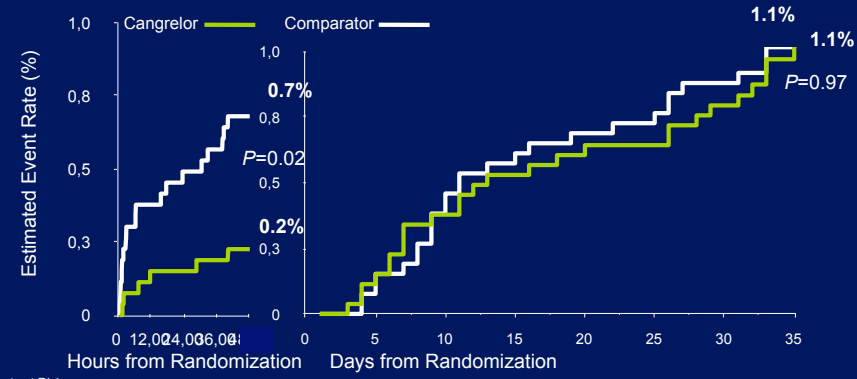
# Landmark Analysis 48-Hour/30-Day Stent Thrombosis



Patients at Risk

|              |      |      |      |      |      |      |      |      |      |      |      |     |
|--------------|------|------|------|------|------|------|------|------|------|------|------|-----|
| Cangrelor:   | 2656 | 2648 | 2646 | 2645 | 2644 | 2634 | 2624 | 2619 | 2617 | 2616 | 2582 | 569 |
| Clopidogrel: | 2645 | 2624 | 2618 | 2617 | 2614 | 2603 | 2589 | 2581 | 2579 | 2577 | 2551 | 559 |

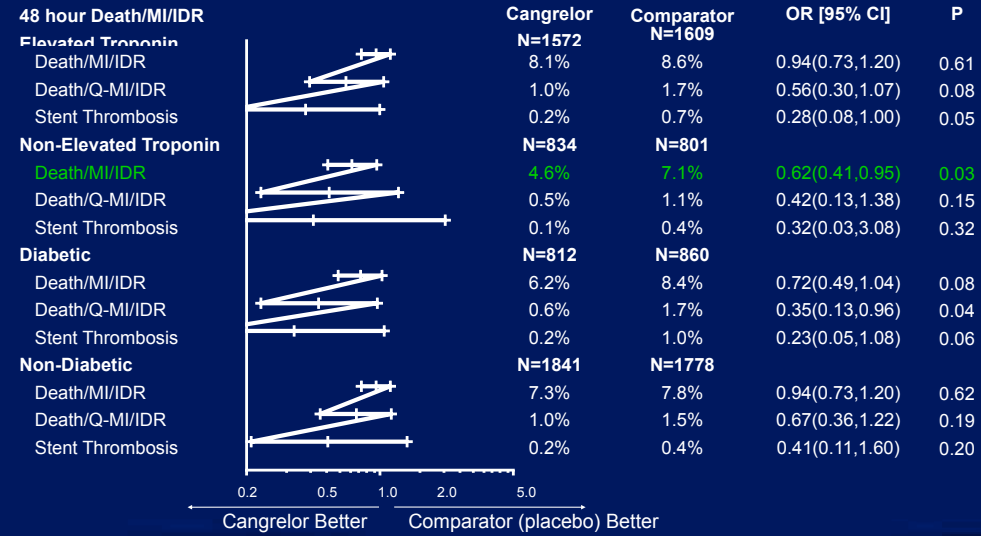
# Landmark Analysis 48-Hour/30-Day Mortality



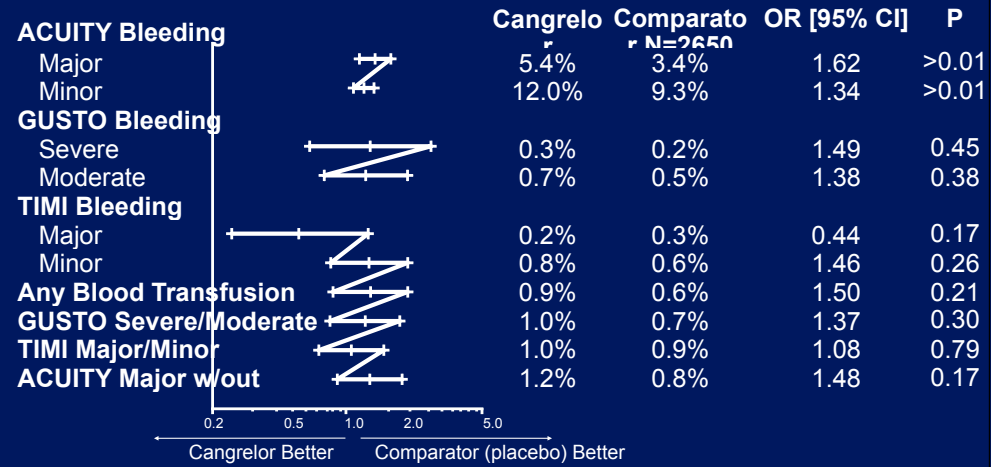
Patients at Risk

|             |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------|------|------|------|------|------|------|------|------|------|------|------|------|
| Cangrelor:  | 2656 | 2652 | 2651 | 2649 | 2648 | 2642 | 2634 | 2629 | 2627 | 2626 | 2614 | 1685 |
| Comparator: | 2645 | 2635 | 2629 | 2627 | 2623 | 2617 | 2604 | 2599 | 2596 | 2595 | 2586 | 1667 |

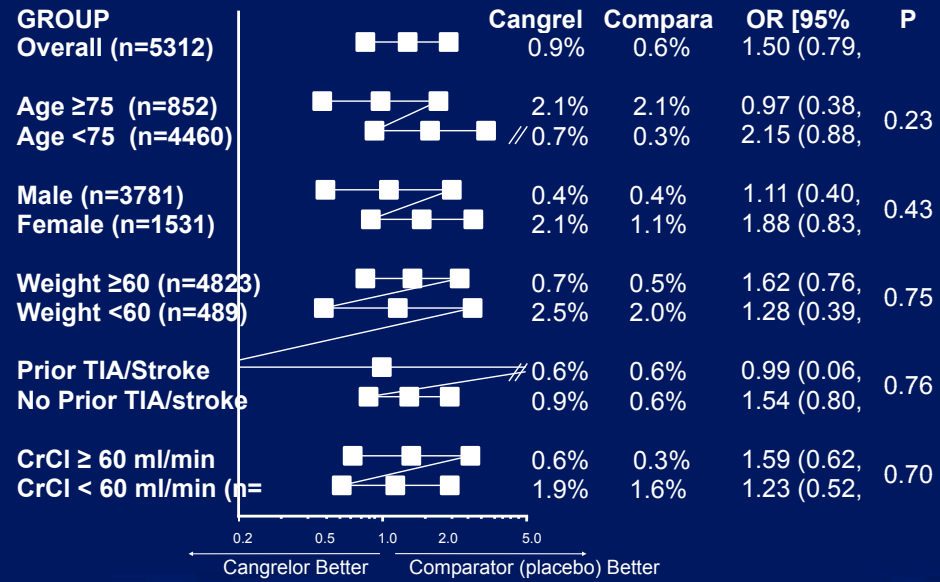
# PLATFORM 48-Hour Efficacy Subgroup Analyses, mITT



# Bleeding Results at 48 Hours



# Transfusions (48 Hours, Non-CABG) High-Risk Subgroups



- Power somewhat limited due to IARC ending trial early
- Short time to PCI increases difficulty of discerning peri-procedural MI, particularly in troponin positive patients
- Primary endpoint negative
  - Secondary/prespecified endpoints hypothesis generating

## Conclusions



- Difference in primary endpoint not statistically significant
- Lower rates of stent thrombosis, mortality biologically plausible
- Effect on “harder” endpoints but not periprocedural MI intriguing
  - Calls into question the definition of periprocedural MI used
- No significant effect on transfusions, even in high risk subgroups
- Groin hematomas increased, not unexpected versus placebo
- Given these results, further study of cangrelor warranted

ORIGINAL ARTICLE

## Intravenous Platelet Blockade with Cangrelor during PCI

Deepak L. Bhatt, M.D., M.P.H., A. Michael Lincoff, M.D.,  
C. Michael Gibson, M.D., Gregg W. Stone, M.D., Steven McNulty, M.S.,  
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Frantisek Tousek, M.D., M. Zubair Jafar, M.D., Jaspal Arneja, M.D.,  
Simona Skerjanec, Pharm.D., and Robert A. Harrington, M.D.,  
for the CHAMPION PLATFORM Investigators\*

Backup Slides



# Summary of Clinical Efficacy



## 48 hour Events

### PLATFORM

Death/MI/IDR\*

Death/Q-MI/IDR

Death/Q-MI/ST

### PCI

Death/MI/IDR\*

Death/Q-MI/IDR

Death/Q-MI/ST

### POOLED

Death/MI/IDR

Death/Q-MI/IDR

Death/Q-MI/ST

OR [95% CI] P value

0.87 (0.71,1.07) 0.17

0.55 (0.33,0.93) 0.02

0.38 (0.20,0.72) 0.002

1.05 (0.89,1.24) 0.57

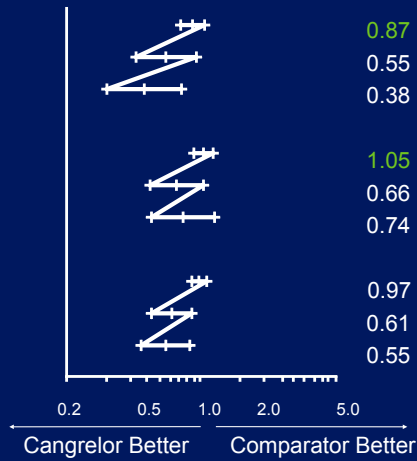
0.66 (0.42,1.05) 0.08

0.74 (0.43,1.27) 0.27

0.97 (0.86,1.11) 0.68

0.61 (0.43,0.86) 0.005

0.55 (0.36,0.83) 0.004

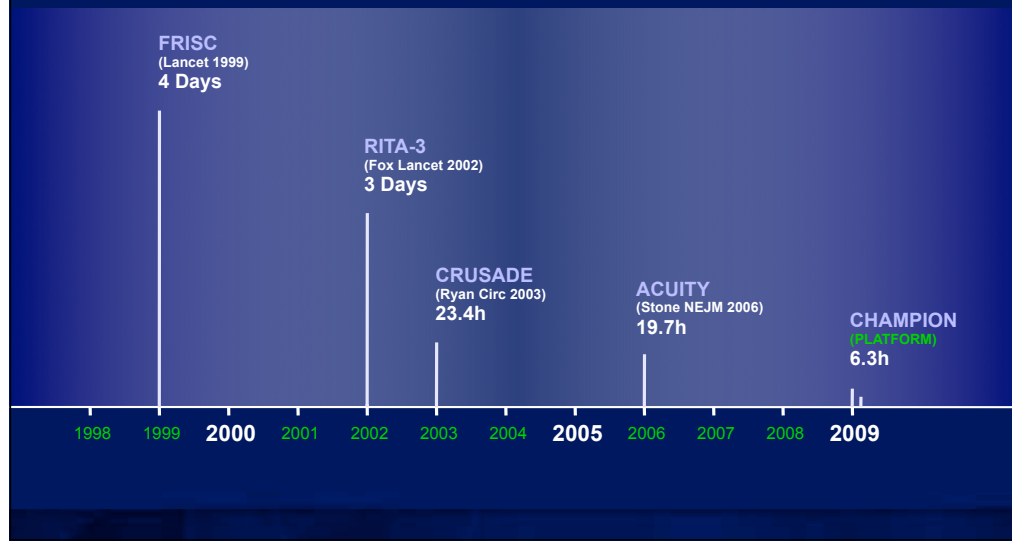


\* Primary Analysis

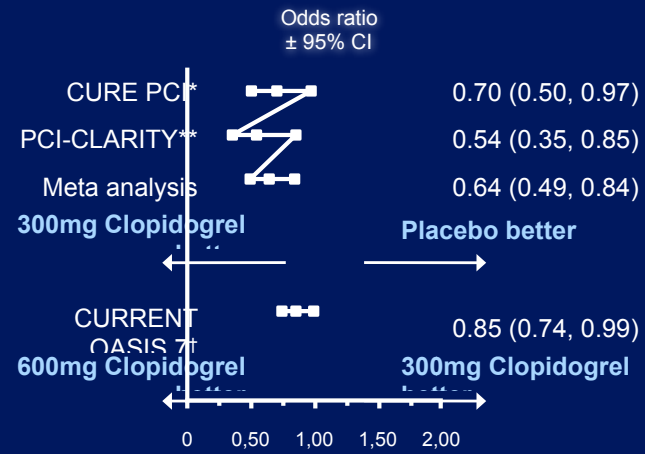
# Time to Cath Lab is Decreasing



- Hospitalization to cath lab

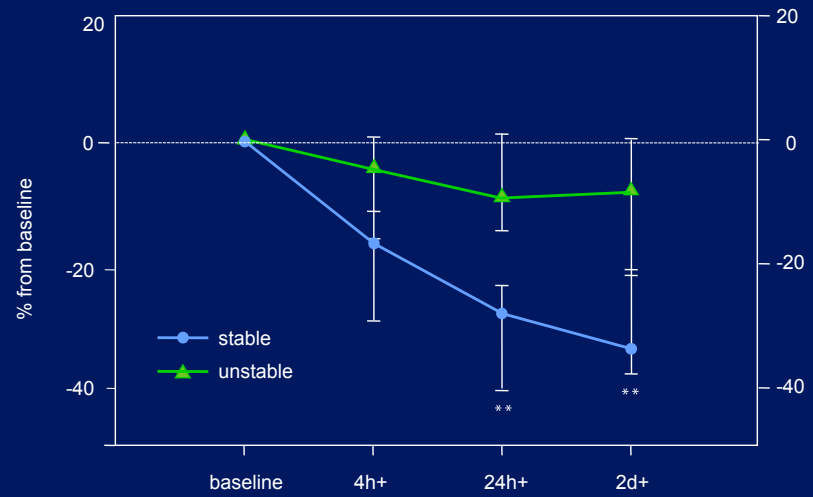


# Benefit of Clopidogrel Pretreatment



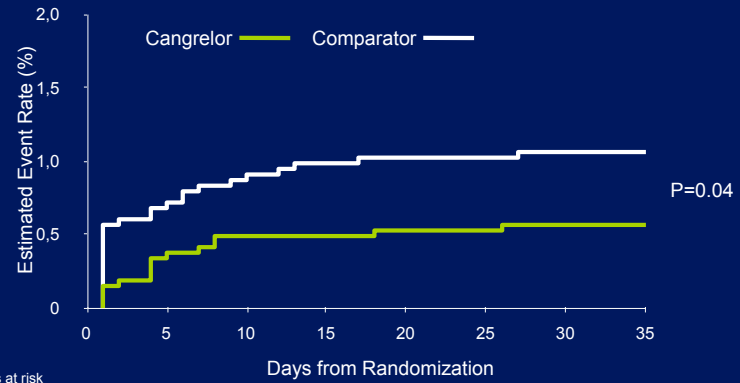
\*Mehta SR, et al *Lancet* 2001;358:527-33. \*\*Sabatine MS, et al *JAMA*. 2005;294:1224-32. † Mehta SR *ESC* 2009

# Clopidogrel Response in AMI Patients – Stable Versus Unstable



Significance between groups: \*\*P < 0.01.

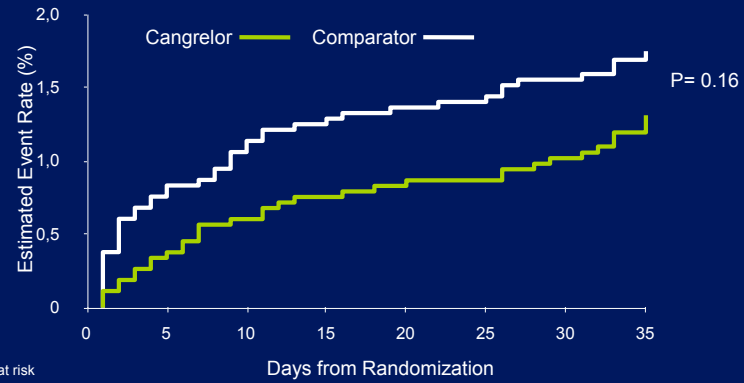
# 30-Day Time-to-Event Analysis Stent Thrombosis



Patients at risk

|            | 0    | 5    | 10   | 15   | 20   | 25   | 30   | 35   |
|------------|------|------|------|------|------|------|------|------|
| Cangrelor  | 2656 | 2637 | 2627 | 2622 | 2620 | 2620 | 2611 | 1687 |
| Comparator | 2645 | 2608 | 2594 | 2587 | 2585 | 2585 | 2579 | 1661 |

# 30-Day Time-to-Event Analysis Mortality



|            | Patients at risk |      |      |      |      |      |      |      |
|------------|------------------|------|------|------|------|------|------|------|
|            | 0                | 5    | 10   | 15   | 20   | 25   | 30   | 35   |
| Cangrelor  | 2656             | 2643 | 2635 | 2630 | 2628 | 2627 | 2615 | 1686 |
| Comparator | 2645             | 2620 | 2607 | 2602 | 2599 | 2598 | 2589 | 1670 |

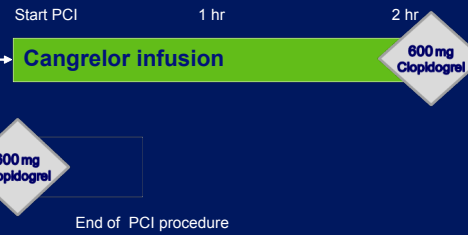
# Trial Design: PCI and PLATFORM



## CHAMPION PCI

- N = 9000
- SA/UA/NSTEMI/STEMI
- Not Thienopyridine Naive

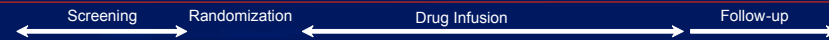
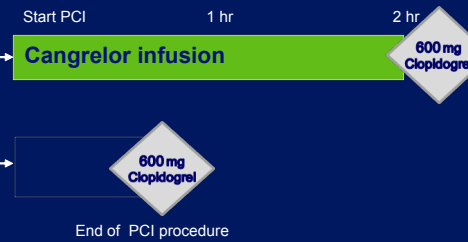
\* Enrollment stopped early by IARC;  
Actual N=8885 (98% of planned)



## CHAMPION PLATFORM

- N = 6400
- SA/UA/NSTEMI
- Thienopyridine Naive

\* Enrollment stopped early by IARC;  
Actual N=5362 (84% of planned)



# Global Implementation



# Global Enrollment - PLATFORM



| PLATFORM       | 5362 (84%) |
|----------------|------------|
| USA            | 1656 (31%) |
| Bulgaria       | 803        |
| Czech Republic | 687        |
| India          | 473        |
| Russia         | 433        |
| South Korea    | 332        |
| South Africa   | 207        |
| Thailand       | 117        |
| Lithuania      | 111        |

| PLATFORM    | 5362 (84%) |
|-------------|------------|
| Brazil      | 98         |
| Georgia     | 90         |
| Argentina   | 82         |
| Belarus     | 64         |
| Slovakia    | 62         |
| Netherlands | 61         |
| New Zealand | 42         |
| Spain       | 39         |
| Canada      | 5          |

# CHAMPION PLATFORM Top 15 USA



| Country | PI          | Hospital  | Enrollment |
|---------|-------------|---|------------|
| USA     | McLaurin    | Anderson Area Medical Center                              | 170        |
| USA     | Jafar       | Hudson Valley Heart Center/Vassar Brothers Medical Center | 123        |
| USA     | Smith       | Trinity Mother Francis Hospital, East Texas Med Center    | 68         |
| USA     | Scott       | University of Tennessee Medical Center                    | 67         |
| USA     | Voeltz      | Emory University Hospital Midtown                         | 63         |
| USA     | Gruberg     | Stony Brook University Hospital                           | 59         |
| USA     | Blankenship | Geisinger Medical Center                                  | 58         |
| USA     | Khan        | Tomball Regional Hospital                                 | 56         |
| USA     | Ferrier     | Rapid City Regional Hospital                              | 50         |
| USA     | Gammon      | The Heart Hospital of Austin                              | 45         |
| USA     | Cannon      | Northern Michigan Hospital                                | 42         |
| USA     | Kao         | Jesse Brown VAMC  | 39         |
| USA     | Gogia       | Anaheim Memorial Medical Center                           | 36         |
| USA     | Srinivasan  | Western PA Hospital                                       | 32         |
| USA     | Istfan      | Wellmont Bristol Regional Medical Center                  | 31         |

# CHAMPION PCI & PLATFORM Top 10 Enrollers



| Country | PI            | Hospital   | Enrollment |
|---------|---------------|--|------------|
| USA     | Jafar         | Hudson Valley Heart Center/Vassar Brothers Medical Center                | 400        |
| Georgia | Shaburishvili | Diagnostic Services Clinic   | 249        |
| India   | Patel         | Krishna Heart and Super Specialty Institute                              | 224        |
| USA     | McLaurin      | Anderson Area Medical Center   | 176        |
| USA     | Gogja         | Western Medical Center Santa Ana   | 174        |
| USA     | Spriggs       | Clearwater Cardiovascular & Interventional Consultant                    | 166        |
| India   | Parikh        | S.A.L.Hospital   | 145        |
| Georgia | Khintibidze   | Tbilisi State Medical University Alexandre Aladashvili University Clinic | 139        |
| USA     | Gruberg       | Stony Brook University Hospital  | 114        |
| Georgia | Chapidze      | Emergency Cardiology Centre  | 105        |

## Trial Committees

### EXECUTIVE/STEERING

Deepak L. Bhatt, MD, MPH: co -PI  
Robert A. Harrington, MD: co -PI  
A. Michael Lincoff, MD  
C. Michael Gibson, MD  
Charles Pollack, MD  
Gilles Montalescot, MD  
Gregg Stone, MD  
Harvey White, DSc  
Kenneth Mahaffey, MD  
Neil Kleiman, MD  
Shaun Goodman, MD

### STEERING

Richard Becker, MD  
Adam Greenbaum, MD  
Dan Simon, MD  
David Lee, MD  
Fred Feit, MD  
Harry Dauerman, MD  
Paul Gurbel, MD  
Peter Berger, MD  
Rajendra Makkar, MD  
Steven Manoukian, MD  
Julia Jorgova, MD  
P. Gabriel Steg, MD  
Petr Widemsky, MD, DrSc

### STEERING

Derek Chew, MD  
Robert Storey, MD  
Walter Desmet, MD  
Fernando Cura, MD  
Howard Hermann, MD  
David Rizik, MD  
Stefano DeServi, MD  
Kurt Huber, MD  
Wouter Jukema, MD  
Heribert Schunkert, MD  
Amadeo Betriu, MD  
William Knopf, MD

## Trial Committees

### IARC

Robert Califf, MD: Chair

Carl J. Pepine, MD

Cyrus Mehta, PhD

James Ware, PhD

Christian Hamm, MD

### DSMB

Frans Van de Werf, MD: Chair

Douglas Weaver, MD

David Faxon, MD

Freek Verheugt, MD

E. Magnus Ohman, MD