



## CHAMPION PCI

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## Relationships with Industry



CHAMPION PCI was sponsored by The Medicines Company which provided funding to the Duke Clinical Research Institute.

For a complete list of RWI for Robert Harrington MD and the Duke Clinical Research Institute, please see: <http://www.dcri.duke.edu/research/coi.jsp>.

For a list of RWI for all co-authors, please see: <http://content.nejm.org/>

Dr Simona Skerjanec is a full-time employee of the sponsor.

## Benefits of ADP Blockade in ACS and PCI Setting



- **Clopidogrel is an excellent drug**
  - Well studied in large RCTs; benefits and risks have been carefully quantified
  - Higher doses (600 mg) appear superior to 300 mg in PCI setting
- **Clopidogrel has well known limitations**
  - Rapidity and predictability/variability of effect
  - Genetic and drug interactions
- **Successful trials with prasugrel and ticagrelor**
  - ADP blockade now a validated therapeutic target
- **Rapidly acting IV ADP blocker may be useful in acute care settings**

# Cangrelor



**Intravenous P2Y<sub>12</sub> inhibitor**

**ADP analogue**

**Plasma half-life: 3-6 minutes**

**Full recovery of platelet function within 60 minutes**

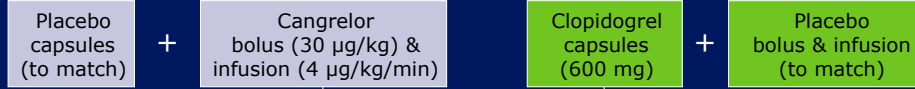
- **Executive Committee**
  - D.L. Bhatt; R.A. Harrington; A.M. Lincoff; C.V. Pollack; C.M. Gibson; G.W. Stone; K.W. Mahaffey; N.S. Kleiman; G. Montalescot; H.D. White; S.G. Goodman
- **Steering Committee**
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- **Clinical Events Committee (CEC)**
- **Data Safety and Monitoring Board (DSMB)**
- **Interim Analysis Review Committee (IARC)**

**Subjects**

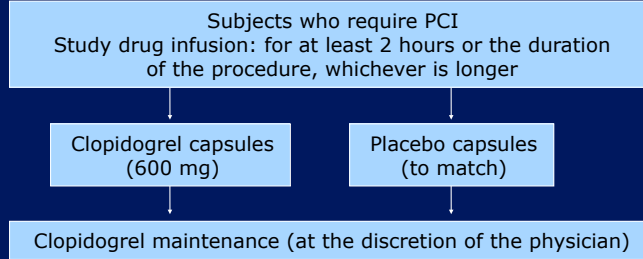
Subjects who require PCI (with or without stent)



1:1 randomization to main treatment groups  
Double blind, double dummy



**Index Procedure**



**Endpoints**

- At 48 hours after randomization—
- 1° efficacy endpoint: composite incidence of all-cause mortality, MI, and IDR
  - 2° efficacy endpoint: incidence of individual components, stroke & abrupt vessel closure
  - Safety endpoints: hemorrhage and transfusion
  - Safety: AEs/SAEs

- **Primary endpoint**
  - 48-hour composite of death, MI, and IDR
- **Secondary endpoints**
  - 48-hour death/MI
  - components: death, MI, IDR
  - stent thrombosis (ARC)
  - exploratory composites: death/QMI/IDR or ST
  - 30-day death/MI/IDR; death at 6 months and 1 year
- **Safety endpoints**
  - Hemorrhage (ACUITY, GUSTO, TIMI criteria), transfusions, SAE/AE

- **Primary Endpoint:**
  - 48-hour composite event rate for death/MI/IDR in mITT SA/UA/NSTEMI population (excluding STE MI)
- **Estimated event rates:**
  - 7% in clopidogrel arm
  - 23% RR reduction
- **Sample size assumptions:**
  - Type I error 0.05
  - Sample size 8000 (4000 per arm) → ~82% power
  - 1000 STEMI patients were planned for a total of 9000
- **Adaptive design features (IARC)**
  - Increase sample; enrich population

- **70% interim analysis**
  - Conditional power for primary efficacy endpoint low
  - No safety issues
  - Opt to continue enrollment until 70% analysis of PLATFORM
- **PLATFORM 70% interim analysis**
  - Conditional power for primary efficacy endpoints low for both trials; no advantage to enrichment strategy
  - May 2009: enrollment terminated into both trials
  - 98% of the planned 9000 patients enrolled into PCI

# Country Enrollment



## Demographics—ITT Population



Baseline characteristics	Cangrelor (N=4433)	Clopidogrel (N=4444)
Age, yrs	62.0 (54.0, 70.0)	62.0 (54.0, 71.0)
Sex, No. (%)		
Male	3275 (73.9)	3209 (72.2)
Female	1158 (26.1)	1235 (27.8)
Race, No. (%)		
White	3658 (82.6)	3626 (81.7)
Asian	311 (7.0)	313 (7.1)
Black	215 (4.9)	239 (5.4)
Weight, kg	84.0 (73.0, 97.0)	84.0 (73.0, 97.0)
Height, cm	172.0 (165.0, 178.0)	172.0 (165.0, 178.0)
Stable angina, No. (%)	668 (15.1)	665 (15.0)
Unstable angina, No. (%)	1097 (24.7)	1088 (24.5)

# Demographics—ITT Population



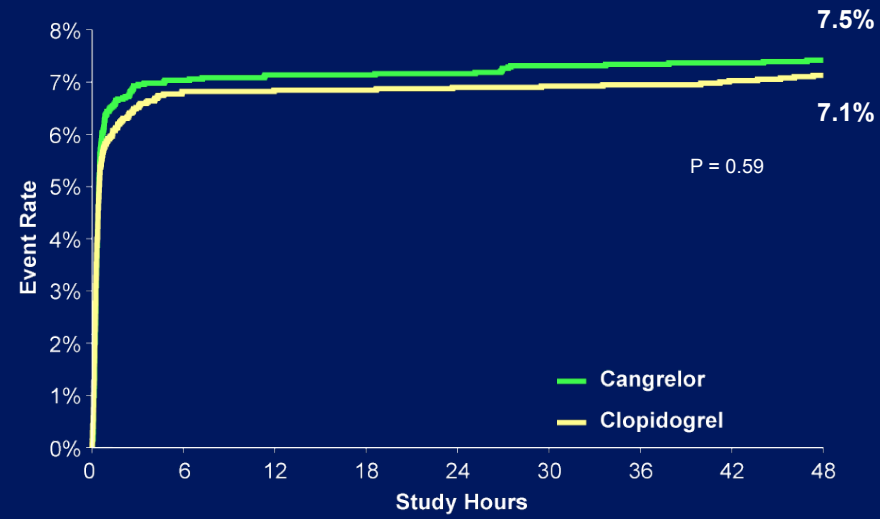
<b>Baseline characteristics</b>	<b>Cangrelor (N=4433)</b>	<b>Clopidogrel (N=4444)</b>
Urgent NSTEMI, No. (%)	639 (14.4)	640 (14.4)
NSTEMI, No. (%)	1542 (34.8)	1542 (34.7)
STEMI, No. (%)	487 (11.0)	509 (11.5)
Medical history, No. (%)		
Diabetes mellitus	1350 (30.5)	1352 (30.5)
Current smoker	1247 (28.5)	1283 (29.1)
Hypertension	3181 (72.1)	3139 (71.0)
Hyperlipidemia	2825 (66.6)	2777 (65.5)
Stroke/TIA	223 (5.1)	227 (5.1)
Family history of CAD	1843 (45.9)	1873 (46.5)
MI	1075 (24.6)	1089 (24.8)
PTCA/PCI	1266 (28.6)	1261 (28.5)
CABG	557 (12.6)	552 (12.4)
Congestive HF	333 (7.6)	338 (7.7)
PAD	323 (7.4)	315 (7.2)

# Procedural Details



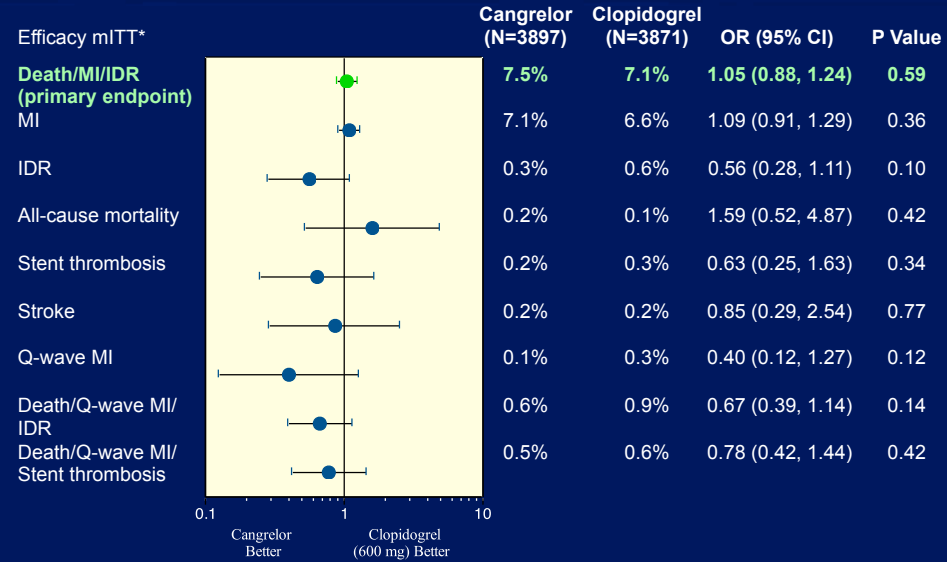
Baseline characteristics	ITT		ITT Without STEMI		ITT With STEMI	
	Cangrelor (N=4433)	Clopidogrel (N=4444)	Cangrelor (N=3946)	Clopidogrel (N=3935)	Cangrelor (N=487)	Clopidogrel (N=509)
Number of target vessels, No. (%)						
1	3836 (88.0)	3796 (87.4)	3406 (87.3)	3360 (86.5)	430 (94.1)	436 (95.2)
2	484 (11.1)	509 (11.7)	457 (11.7)	488 (12.6)	27 (5.9)	21 (4.6)
3	38 (0.9)	36 (0.8)	38 (1.0)	35 (0.9)	0 (0.0)	1 (0.2)
Drug-eluting stent, No. (%)	2581 (59.2)	2560 (59.0)	2422 (62.1)	2383 (61.4)	159 (34.8)	177 (38.6)
Non-drug-eluting stent, No. (%)	1640 (37.6)	1635 (37.7)	1367 (35.0)	1380 (35.5)	273 (59.7)	255 (55.7)

# Primary Endpoint: 48-hour Death/MI/IDR (MITT)



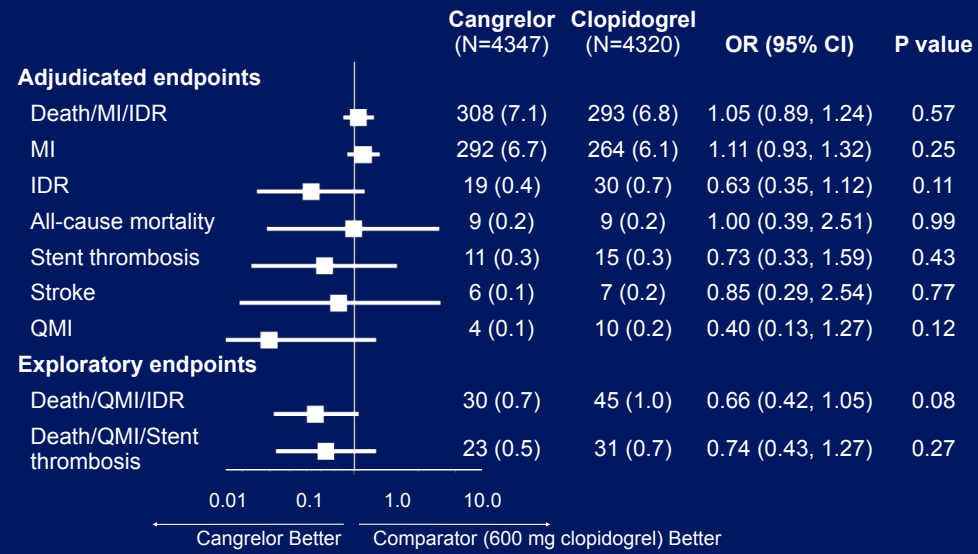
Cangrelor:	3897	3623	3619	3619	3614	3606	3604	3603	3599
Clopidogrel:	3871	3607	3606	3606	3602	3599	3598	3595	3588

# Efficacy Endpoints at 48 hours



\*mITT= modified intent to treat population (patients with PCI and study drug)

# 48-hour Endpoints for ITT with STEMI Population



# Bleeding

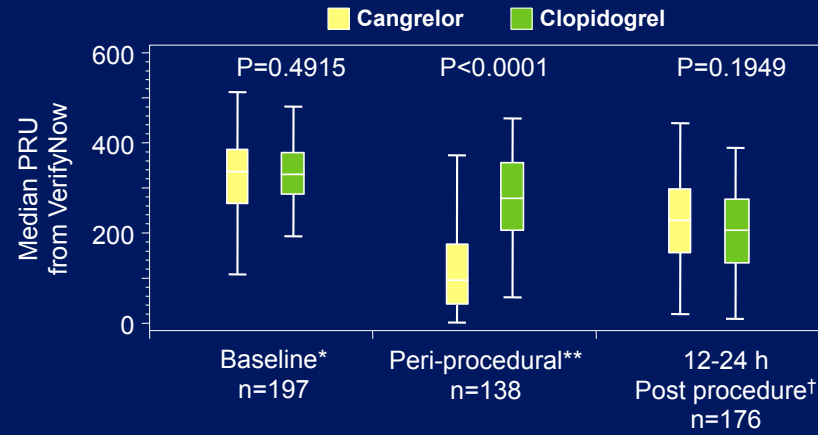


	Cangrelor	Clopidogrel	OR (95% CI)	P Value
Any blood transfusion	46 (1.1)	42 (1.0)	1.09 (0.72, 1.67)	0.68
<b>Bleed scoring criteria:</b>				
ACUITY criteria				
Minor bleeding	768 (17.6)	663 (15.2)	1.19 (1.06, 1.33)	0.003
Major bleeding	158 (3.6)	126 (2.9)	1.26 (0.99, 1.60)	0.06
GUSTO criteria				
Mild bleeding	858 (19.6)	739 (16.9)	1.20 (1.07, 1.34)	0.001
Moderate bleeding	41 (0.9)	34 (0.8)	1.21 (0.76, 1.90)	0.42
Severe/life-threatening 0.82 bleeding	10 (0.2)	11 (0.3)	0.91 (0.39, 2.14)	
TIMI criteria				
Minor bleeding	36 (0.8)	26 (0.6)	1.39 (0.84, 2.30)	0.21
Major bleeding	19 (0.4)	14 (0.3)	1.36 (0.68, 2.70)	0.39

# Platelet Substudy Results



- More robust platelet inhibition with cangrelor during infusion
- No evidence of attenuation of clopidogrel effect at 12-24 hours



\*\*Baseline- Before the first infusion.  
\*\*Peri-procedural- During study drug/placebo infusion  
† Post procedure - 1st sample within 12 to 24 hours relative to 1st Infusion.

## Non-inferiority Analysis



Using standard non-inferiority methods, we estimate that cangrelor preserves at least 62% (>50%) of the effect of clopidogrel 600 mg vs placebo.

PCI-CURE	0.70 (0.50, 0.97)	(300 mg vs placebo)
CLARITY	0.54 (0.35, 0.85)	(300 mg vs placebo)
CURRENT-OASIS 7	0.85 (0.74, 0.99)	(600 mg vs 300mg)
CHAMPION PCI	1.04 (0.90, 1.21)	(cangrelor vs 600 mg)

## Limitations



- Trial stopped early for futility
- Neutral result renders all other analyses exploratory and hypothesis-generating
- Challenges with diagnosing re-MI when baseline biomarkers elevated and limited pre-PCI samples to determine marker re-elevation
- Optimal length of IV infusion unknown

- Cangrelor was not superior to 600 mg clopidogrel in moderate to high risk patients undergoing PCI.
- Using standard methods, we estimate that cangrelor appears to be non-inferior to 600 mg clopidogrel.
- Platelet function testing revealed that cangrelor provides very rapid ADP blockade and did not interfere with post PCI clopidogrel effect.
- There was an increase in ACUITY minor and GUSTO mild bleeding with cangrelor though no increase in the need for blood transfusion with cangrelor compared with clopidogrel.
- Several post hoc exploratory endpoints and a combined analysis with CHAMPION PLATFORM suggest that cangrelor warrants consideration of further investigation.

ORIGINAL ARTICLE

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