

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Bhatt DL, Lincoff AM, Gibson CM, et al. Intravenous platelet blockade with cangrelor during PCI. N Engl J Med 2009;361:2330-41. DOI: 10.1056/NEJMoa0908629.

## Appendices

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**Online Table 1.** 30-day endpoints for ITT, MITT, and Safety Populations

	<b><u>ITT</u></b>			
	<b>Cangrelor</b>	<b>Clopidogrel</b>	<b>OR (95% CI)</b>	<b>P Value</b>
	<b>(N=2693)</b>	<b>(N=2669)</b>		
<b>Adjudicated endpoints</b>				
Death/MI/IDR	230 (8.6)	254 (9.6)	0.89 (0.73, 1.07)	0.20
MI	190 (7.1)	202 (7.6)	0.92 (0.75, 1.14)	0.45
IDR	37 (1.4)	49 (1.8)	0.74 (0.48, 1.14)	0.18
All-cause mortality	36 (1.3)	47 (1.8)	0.75 (0.49, 1.17)	0.20
Stent thrombosis	15 (0.6)	29 (1.1)	0.51 (0.27, 0.95)	0.03
Q-wave MI	8 (0.3)	15 (0.6)	0.53 (0.22, 1.24)	0.14
<b>Exploratory endpoints</b>				
Death/Q-wave MI/IDR	69 (2.6)	94 (3.5)	0.72 (0.52, 0.98)	0.04
Death/Q-wave MI/Stent thrombosis	51 (1.9)	77 (2.9)	0.65 (0.45, 0.93)	0.02
	<b><u>MITT</u></b>			
	<b>Cangrelor</b>	<b>Clopidogrel</b>	<b>OR (95% CI)</b>	<b>P Value</b>
	<b>(N=2656)</b>	<b>(N=2645)</b>		
<b>Adjudicated endpoints</b>				
Death/MI/IDR	226 (8.5)	249 (9.5)	0.89 (0.74, 1.08)	0.24
MI	189 (7.1)	201 (7.6)	0.93 (0.76, 1.14)	0.48
IDR	37 (1.4)	46 (1.7)	0.80 (0.52, 1.23)	0.31
All-cause mortality	33 (1.2)	45 (1.7)	0.73 (0.46, 1.14)	0.16
Stent thrombosis	15 (0.6)	28 (1.1)	0.53 (0.28, 0.99)	0.05

Q-wave MI	8 (0.3)	14 (0.5)	0.57 (0.24, 1.35)	0.20
<b>Exploratory endpoints</b>				
Death/Q-wave MI/IDR	66 (2.5)	89 (3.4)	0.73 (0.53, 1.01)	0.06
Death/Q-wave MI/Stent thrombosis	48 (1.8)	73 (2.8)	0.65 (0.45, 0.94)	0.02

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**Safety**

	<b>Cangrelor</b>	<b>Clopidogrel</b>	<b>OR (95% CI)</b>	<b>P Value</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>		
<b>Adjudicated endpoints</b>				
Death/MI/IDR	226 (8.5)	251 (9.5)	0.88 (0.73, 1.07)	0.20
MI	188 (7.1)	203 (7.7)	0.91 (0.74, 1.12)	0.39
IDR	37 (1.4)	47 (1.8)	0.78 (0.50, 1.20)	0.26
All-cause mortality	34 (1.3)	45 (1.7)	0.75 (0.48, 1.17)	0.20
Stent thrombosis	15 (0.6)	28 (1.1)	0.53 (0.28, 0.99)	0.05
Q-wave MI	8 (0.3)	15 (0.6)	0.53 (0.22, 1.25)	0.15
<b>Exploratory endpoints</b>				
Death/Q-wave MI/IDR	67 (2.5)	90 (3.4)	0.73 (0.53, 1.01)	0.06
Death/Q-wave MI/Stent thrombosis	49 (1.8)	74 (2.8)	0.65 (0.45, 0.94)	0.02

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Variables are presented as no. (%) unless otherwise indicated. CI denotes confidence interval; IDR, ischemia-driven revascularization; ITT, intent to treat; MI, myocardial infarction; MITT, modified intent to treat; OR, odds ratio.

**Online Table 2.** 48-hour adverse events by body system and preferred term for the Safety

Population

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
<b>Blood and lymphatic system disorders</b>		
Anaemia	4 (0.1)	2 (0.1)
Eosinophilia	1 (0.0)	0 (0.0)
Haemorrhagic anaemia	1 (0.0)	0 (0.0)
Leukocytosis	3 (0.1)	2 (0.1)
Microcytic anaemia	1 (0.0)	0 (0.0)
Thrombocytopenia	2 (0.1)	0 (0.0)
<b>Cardiac disorders</b>		
Acute left ventricular failure	0 (0.0)	1 (0.0)
Angina pectoris	11 (0.4)	17 (0.6)
Angina unstable	2 (0.1)	2 (0.1)
Arrhythmia	0 (0.0)	1 (0.0)
Atrial fibrillation	7 (0.3)	8 (0.3)
Atrial flutter	2 (0.1)	2 (0.1)
Atrioventricular block	1 (0.0)	2 (0.1)
Atrioventricular block first degree	1 (0.0)	0 (0.0)
Atrioventricular block second degree	0 (0.0)	1 (0.0)
Atrioventricular block third degree	5 (0.2)	0 (0.0)
Bradycardia	10 (0.4)	14 (0.5)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Cardiac arrest	1 (0.0)	3 (0.1)
Cardiac failure	3 (0.1)	1 (0.0)
Cardiac failure acute	2 (0.1)	0 (0.0)
Cardiac failure congestive	4 (0.1)	4 (0.1)
Cardiac flutter	0 (0.0)	1 (0.0)
Cardiac tamponade	0 (0.0)	1 (0.0)
Cardiogenic shock	6 (0.2)	11 (0.4)
Cardiomegaly	0 (0.0)	1 (0.0)
Coronary artery dissection	10 (0.4)	7 (0.3)
Coronary artery embolism	0 (0.0)	1 (0.0)
Coronary artery occlusion	3 (0.1)	5 (0.2)
Coronary artery perforation	2 (0.1)	0 (0.0)
Coronary artery thrombosis	1 (0.0)	1 (0.0)
Electromechanical dissociation	1 (0.0)	3 (0.1)
Extrasystoles	0 (0.0)	1 (0.0)
Ischaemic cardiomyopathy	0 (0.0)	1 (0.0)
Left ventricular failure	3 (0.1)	3 (0.1)
Mitral valve incompetence	1 (0.0)	0 (0.0)
Myocardial infarction	1 (0.0)	1 (0.0)
Myocardial rupture	0 (0.0)	1 (0.0)
Nodal arrhythmia	3 (0.1)	0 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Nodal rhythm	1 (0.0)	0 (0.0)
Palpitations	2 (0.1)	5 (0.2)
Pericarditis	0 (0.0)	1 (0.0)
Sick sinus syndrome	1 (0.0)	0 (0.0)
Sinus arrest	1 (0.0)	0 (0.0)
Sinus bradycardia	1 (0.0)	2 (0.1)
Sinus tachycardia	1 (0.0)	2 (0.1)
Supraventricular extrasystoles	1 (0.0)	0 (0.0)
Supraventricular tachycardia	3 (0.1)	1 (0.0)
Tachyarrhythmia	1 (0.0)	0 (0.0)
Tachycardia	3 (0.1)	3 (0.1)
Torsade de pointes	0 (0.0)	2 (0.1)
Ventricular arrhythmia	1 (0.0)	0 (0.0)
Ventricular dysfunction	0 (0.0)	1 (0.0)
Ventricular extrasystoles	4 (0.1)	4 (0.1)
Ventricular fibrillation	6 (0.2)	7 (0.3)
Ventricular tachycardia	10 (0.4)	11 (0.4)
Congenital, familial and genetic disorders		
Myocardial bridging	0 (0.0)	1 (0.0)
Ear and labyrinth disorders		
Ear haemorrhage	1 (0.0)	0 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Tinnitus	0 (0.0)	1 (0.0)
Vertigo	3 (0.1)	2 (0.1)
Eye disorders		
Diplopia	0 (0.0)	1 (0.0)
Vision blurred	0 (0.0)	1 (0.0)
Visual disturbance	1 (0.0)	0 (0.0)
Gastrointestinal disorders		
Abdominal discomfort	2 (0.1)	3 (0.1)
Abdominal pain	9 (0.3)	8 (0.3)
Abdominal pain lower	2 (0.1)	1 (0.0)
Abdominal pain upper	4 (0.1)	2 (0.1)
Abdominal tenderness	1 (0.0)	0 (0.0)
Barrett's oesophagus	0 (0.0)	1 (0.0)
Constipation	6 (0.2)	4 (0.1)
Diarrhoea	6 (0.2)	3 (0.1)
Duodenitis	1 (0.0)	0 (0.0)
Duodenogastric reflux	1 (0.0)	0 (0.0)
Dyspepsia	10 (0.4)	8 (0.3)
Enteritis	1 (0.0)	0 (0.0)
Epigastric discomfort	1 (0.0)	0 (0.0)
Erosive oesophagitis	1 (0.0)	0 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Gastritis	1 (0.0)	0 (0.0)
Nausea	71 (2.6)	65 (2.4)
Retroperitoneal haemorrhage	1 (0.0)	0 (0.0)
Stomach discomfort	1 (0.0)	0 (0.0)
Vomiting	37 (1.4)	31 (1.2)
General disorders and administration site conditions		
Asthenia	4 (0.1)	3 (0.1)
Catheter site pain	3 (0.1)	5 (0.2)
Chest discomfort	12 (0.4)	11 (0.4)
Chest pain	73 (2.7)	67 (2.5)
Chills	1 (0.0)	3 (0.1)
Discomfort	1 (0.0)	3 (0.1)
Fatigue	4 (0.1)	1 (0.0)
Feeling abnormal	0 (0.0)	1 (0.0)
Hyperthermia	0 (0.0)	1 (0.0)
Infusion site bruising	0 (0.0)	1 (0.0)
Infusion site extravasation	1 (0.0)	3 (0.1)
Infusion site inflammation	0 (0.0)	1 (0.0)
Infusion site pain	0 (0.0)	1 (0.0)
Infusion site phlebitis	0 (0.0)	1 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Injection site phlebitis	0 (0.0)	1 (0.0)
Malaise	2 (0.1)	0 (0.0)
Multi-organ failure	0 (0.0)	1 (0.0)
Non-cardiac chest pain	7 (0.3)	8 (0.3)
Oedema peripheral	1 (0.0)	1 (0.0)
Pain	14 (0.5)	7 (0.3)
Paradoxical drug reaction	0 (0.0)	1 (0.0)
Puncture site pain	21 (0.8)	28 (1.0)
Pyrexia	36 (1.3)	20 (0.7)
Vessel puncture site haematoma	1 (0.0)	0 (0.0)
Hepatobiliary disorders		
Hepatomegaly	0 (0.0)	1 (0.0)
Hyperbilirubinaemia	1 (0.0)	2 (0.1)
Immune system disorders		
Hypersensitivity	2 (0.1)	0 (0.0)
Infections and infestations		
Bacterial sepsis	0 (0.0)	1 (0.0)
Bronchitis acute	1 (0.0)	0 (0.0)
Bronchopneumonia	1 (0.0)	0 (0.0)
Catheter sepsis	1 (0.0)	0 (0.0)
Endocarditis	0 (0.0)	1 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Gastroenteritis	0 (0.0)	1 (0.0)
Lung infection	0 (0.0)	1 (0.0)
Pneumonia	4 (0.1)	2 (0.1)
Pyelonephritis chronic	0 (0.0)	1 (0.0)
Respiratory tract infection	0 (0.0)	2 (0.1)
Urinary tract infection	6 (0.2)	0 (0.0)
<b>Injury, poisoning and procedural complications</b>		
Arterial injury	0 (0.0)	1 (0.0)
Brain contusion	1 (0.0)	0 (0.0)
Device breakage	1 (0.0)	0 (0.0)
Excoriation	0 (0.0)	2 (0.1)
Fall	1 (0.0)	0 (0.0)
Head injury	1 (0.0)	0 (0.0)
Incorrect dose administered	1 (0.0)	0 (0.0)
Post procedural discomfort	0 (0.0)	1 (0.0)
Post procedural haematuria	0 (0.0)	1 (0.0)
Post procedural headache	1 (0.0)	0 (0.0)
Post procedural nausea	1 (0.0)	0 (0.0)
Post procedural swelling	1 (0.0)	1 (0.0)
Post procedural vomiting	1 (0.0)	0 (0.0)
Procedural hypertension	1 (0.0)	3 (0.1)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Procedural hypotension	0 (0.0)	2 (0.1)
Procedural pain	6 (0.2)	0 (0.0)
Skin laceration	1 (0.0)	0 (0.0)
Thrombosis in device	1 (0.0)	2 (0.1)
Urinary retention postoperative	0 (0.0)	1 (0.0)
Vascular procedure complication	2 (0.1)	3 (0.1)
<b>Investigations</b>		
Alanine aminotransferase increased	0 (0.0)	1 (0.0)
Anticoagulation drug level below therapeutic	1 (0.0)	0 (0.0)
Aspartate aminotransferase increased	3 (0.1)	2 (0.1)
Blood bilirubin increased	1 (0.0)	2 (0.1)
Blood creatine phosphokinase increased	0 (0.0)	1 (0.0)
Blood creatinine increased	2 (0.1)	3 (0.1)
Blood glucose increased	3 (0.1)	0 (0.0)
Blood potassium decreased	1 (0.0)	5 (0.2)
Blood pressure decreased	2 (0.1)	0 (0.0)
Blood pressure increased	4 (0.1)	2 (0.1)
Blood thyroid stimulating hormone increased	1 (0.0)	0 (0.0)
Body temperature increased	0 (0.0)	4 (0.1)
Cardiac enzymes increased	3 (0.1)	1 (0.0)
Cardiac output decreased	1 (0.0)	0 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Electrocardiogram change	1 (0.0)	0 (0.0)
Glucose urine present	0 (0.0)	1 (0.0)
Haematocrit decreased	0 (0.0)	1 (0.0)
Heart rate increased	0 (0.0)	1 (0.0)
Hepatic enzyme increased	1 (0.0)	1 (0.0)
Liver function test abnormal	3 (0.1)	1 (0.0)
Platelet count decreased	0 (0.0)	1 (0.0)
Red blood cell sedimentation rate increased	1 (0.0)	0 (0.0)
Troponin increased	0 (0.0)	1 (0.0)
Urine output decreased	0 (0.0)	1 (0.0)
White blood cell count increased	3 (0.1)	0 (0.0)
<b>Metabolism and nutrition disorders</b>		
Anorexia	0 (0.0)	1 (0.0)
Diabetes mellitus	0 (0.0)	1 (0.0)
Diabetes mellitus inadequate control	1 (0.0)	0 (0.0)
Electrolyte imbalance	0 (0.0)	1 (0.0)
Fluid imbalance	1 (0.0)	0 (0.0)
Hyperglycaemia	3 (0.1)	1 (0.0)
Hyperlipidaemia	1 (0.0)	0 (0.0)
Hypoglycaemia	2 (0.1)	1 (0.0)
Hypokalaemia	7 (0.3)	2 (0.1)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
<b>Musculoskeletal and connective tissue disorders</b>		
Arthralgia	4 (0.1)	4 (0.1)
Arthritis	1 (0.0)	0 (0.0)
Back pain	90 (3.3)	83 (3.1)
Groin pain	1 (0.0)	0 (0.0)
Muscle spasms	2 (0.1)	0 (0.0)
Muscular weakness	1 (0.0)	0 (0.0)
Musculoskeletal chest pain	0 (0.0)	3 (0.1)
Musculoskeletal pain	3 (0.1)	13 (0.5)
Musculoskeletal stiffness	0 (0.0)	1 (0.0)
Neck pain	2 (0.1)	2 (0.1)
Pain in extremity	14 (0.5)	14 (0.5)
Sacral pain	1 (0.0)	0 (0.0)
<b>Nervous system disorders</b>		
Disturbance in attention	1 (0.0)	0 (0.0)
Dizziness	9 (0.3)	9 (0.3)
Dizziness postural	0 (0.0)	1 (0.0)
Haemorrhage intracranial	1 (0.0)	0 (0.0)
Headache	59 (2.2)	67 (2.5)
Hypoaesthesia	4 (0.1)	4 (0.1)
Hypotonia	0 (0.0)	2 (0.1)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Incoherent	0 (0.0)	1 (0.0)
Lethargy	0 (0.0)	1 (0.0)
Loss of consciousness	1 (0.0)	0 (0.0)
Metabolic encephalopathy	0 (0.0)	1 (0.0)
Migraine	2 (0.1)	0 (0.0)
Neuralgia	1 (0.0)	0 (0.0)
Paraesthesia	3 (0.1)	4 (0.1)
Psychomotor hyperactivity	3 (0.1)	2 (0.1)
Somnolence	0 (0.0)	1 (0.0)
Syncope	3 (0.1)	2 (0.1)
Syncope vasovagal	13 (0.5)	4 (0.1)
Transient ischaemic attack	0 (0.0)	4 (0.1)
Vascular encephalopathy	1 (0.0)	0 (0.0)
<b>Psychiatric disorders</b>		
Abnormal dreams	0 (0.0)	1 (0.0)
Aggression	1 (0.0)	0 (0.0)
Agitation	3 (0.1)	3 (0.1)
Alcohol withdrawal syndrome	0 (0.0)	1 (0.0)
Anxiety	13 (0.5)	3 (0.1)
Confusional state	5 (0.2)	2 (0.1)
Crying	0 (0.0)	1 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Delirium	2 (0.1)	3 (0.1)
Disorientation	1 (0.0)	1 (0.0)
Insomnia	10 (0.4)	15 (0.6)
Mental status changes	1 (0.0)	0 (0.0)
Nervousness	0 (0.0)	1 (0.0)
Panic attack	1 (0.0)	1 (0.0)
<b>Renal and urinary disorders</b>		
Bladder distension	0 (0.0)	1 (0.0)
Bladder spasm	1 (0.0)	0 (0.0)
Calyceal diverticulum	0 (0.0)	1 (0.0)
Dysuria	4 (0.1)	3 (0.1)
Incontinence	0 (0.0)	1 (0.0)
Nephropathy toxic	2 (0.1)	0 (0.0)
Proteinuria	0 (0.0)	1 (0.0)
Renal failure	3 (0.1)	2 (0.1)
Renal failure acute	1 (0.0)	1 (0.0)
Renal failure chronic	1 (0.0)	0 (0.0)
Renal impairment	0 (0.0)	1 (0.0)
Urinary retention	5 (0.2)	1 (0.0)
<b>Reproductive system and breast disorders</b>		
Benign prostatic hyperplasia	0 (0.0)	1 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
<b>Respiratory, thoracic and mediastinal disorders</b>		
Acute pulmonary oedema	3 (0.1)	0 (0.0)
Atelectasis	0 (0.0)	1 (0.0)
Bronchospasm	1 (0.0)	1 (0.0)
Chronic obstructive pulmonary disease	0 (0.0)	1 (0.0)
Cough	3 (0.1)	6 (0.2)
Dyspnoea	37 (1.4)	14 (0.5)
Laryngeal oedema	0 (0.0)	1 (0.0)
Nasal discomfort	1 (0.0)	0 (0.0)
Pharyngolaryngeal pain	0 (0.0)	1 (0.0)
Pulmonary congestion	0 (0.0)	1 (0.0)
Pulmonary embolism	0 (0.0)	1 (0.0)
Pulmonary fibrosis	0 (0.0)	1 (0.0)
Pulmonary oedema	6 (0.2)	6 (0.2)
Rales	0 (0.0)	4 (0.1)
Respiratory failure	1 (0.0)	0 (0.0)
Rhinorrhoea	1 (0.0)	0 (0.0)
Sleep apnoea syndrome	0 (0.0)	1 (0.0)
<b>Skin and subcutaneous tissue disorders</b>		
Angioneurotic oedema	1 (0.0)	0 (0.0)
Cold sweat	0 (0.0)	1 (0.0)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Dermatitis allergic	0 (0.0)	1 (0.0)
Erythema	0 (0.0)	1 (0.0)
Hyperhidrosis	2 (0.1)	3 (0.1)
Pruritus	2 (0.1)	3 (0.1)
Psoriasis	0 (0.0)	1 (0.0)
Purpura	1 (0.0)	0 (0.0)
Rash	8 (0.3)	4 (0.1)
Rash erythematous	1 (0.0)	1 (0.0)
Rash generalised	0 (0.0)	1 (0.0)
Skin ulcer	1 (0.0)	0 (0.0)
Swelling face	1 (0.0)	0 (0.0)
Urticaria	0 (0.0)	1 (0.0)
<b>Surgical and medical procedures</b>		
Pacemaker generated rhythm	0 (0.0)	1 (0.0)
<b>Vascular disorders</b>		
Accelerated hypertension	1 (0.0)	1 (0.0)
Arteriovenous fistula	0 (0.0)	2 (0.1)
Embolism	1 (0.0)	1 (0.0)
Flushing	1 (0.0)	0 (0.0)
Haematoma	3 (0.1)	0 (0.0)
Hypertension	28 (1.0)	22 (0.8)

	<b>Cangrelor</b>	<b>Clopidogrel</b>
	<b>(N=2662)</b>	<b>(N=2650)</b>
Hypertensive crisis	1 (0.0)	0 (0.0)
Hypertensive emergency	1 (0.0)	0 (0.0)
Hypotension	42 (1.6)	37 (1.4)
Orthostatic hypotension	2 (0.1)	0 (0.0)
Peripheral ischaemia	0 (0.0)	1 (0.0)
Phlebitis	2 (0.1)	1 (0.0)
Phlebitis superficial	1 (0.0)	0 (0.0)
Reperfusion injury	3 (0.1)	3 (0.1)
Shock	0 (0.0)	1 (0.0)
Thrombosis	1 (0.0)	0 (0.0)
Vascular pseudoaneurysm	0 (0.0)	1 (0.0)

## **Online Figure Legends**

**Figure 1.** CONSORT diagram.

**Figure 2.** Transfusion rates for all patients (including coronary artery bypass graft) in subgroups at high risk of bleeding.

# CHAMPION PLATFORM CONSORT DIAGRAM



