Table1 - Summary of evaluated clinical trials

Study	Purpose	Study Design	# of Subjects	Location
PCI -CURE August 2001	To test the hypothesis that pre-treatment with clopidogrel before PCI is superior to placebo in preventing major ischemic events afterward & that long-term (up to1year) treatment with clopidogrel would result in additional benefit.	Prospective Subset of double-blind, placebo controlled randomized (CURE) trial	CURE=12,562 PCICURE=2,658	International Multicenter
CREDO November 2002	To evaluate benefit of long-term (12 month) treatment with clopidogrel after PCI & to determine the benefit of initiating clopidogrel with a pre-procedure loading dose, both in addition to aspirin therapy.	Randomized, double-blind, placebo-controlled	N=2,116	US and Canada Multicenter
TARGET Subset May 2003 (TARGET June 2001)	To determine if clopidogrel treatment initiated prior to PCI improved clinical outcomes among patients receiving aspirin and a glycoprotein IIb/IIIa inhibitor.	Prospective Subset of double-blind, randomized, head-to-head (TARGET) trial	N=4,808	International Multicenter
"CBRACE" May 2002	To evaluate the effects of a loading dose of clopidogrel (in addition to chronic aspirin therapy) given the day prior to PCI in an unselected population.	Non-randomized comparison of consecutive patients	N=1,430	Single Center (Sweden)
"LEC" July 2004	To determine the effect of pre-treatment with clopidogrel in patients undergoing elective stent implantation.	Randomized Physicians blinded to drug assignment during procedure and assessment of follow-up data	N=203	Single Center (Amsterdam)

STUDY	Inclusion Criteria	Exclusion Criteria
PCI-CURE (From CURE)	-Symptoms of ACS w/in past 24hr w/o ST segment elevation of 1mm on EKG -Other evidence of new ischemia (on EKG) or cardiac enzymes of >2X upper limit	-Contraindications to antithrombotic or antiplatelet therapy -High risk of bleeding -NYHA Class IV heart failure -Required long-term oral anticoagulant -Undergone PCI or CABG w/in past 3 mo -Received GP IIb/IIIa inhibitor <3 days before randomization
CREDO	-Symptomatic coronary artery disease w/objective evidence of ischemia -Referred for PCI -At least 21 yrs of age	-Contraindications to antithrombotic/anti- platelet therapy ->50% stenosis of L main coronary artery -Coronary anatomy not amendable to stent placement - Failed coronary intervention in the previous 2 weeks - Persistent ST elevation w/in 24 hours prior to randomization - Received GP IIb/IIIa inhibitior w/in 7 days, clopidogrel, w/in 10 days, or thrombolytics w/in 24hr
TARGET	-Scheduled to undergo PCI stenting procedure of a newly stenotic or restenotic atherosclerotic lesion in a native vessel or bypass graft -Lesions w/stenosis of >70% had to be amenable to stenting	-Cardiogenic shock -Acute MI w/ST segment elevation -Serum creatinine >2.5mg/dL -Ongoing bleeding or bleeding diathesis -Platelet count <120,000/mm3
"CBRACE"	-Consecutive patients undergoing PCI	-PCI in the setting of acute myocardial infarction (AMI)
"LEC"	-Patients scheduled to undergo elective PCI with stent implantation	-Primary intervention for AMI or other emergency procedures -Elevated baseline troponin I or CK-MB levels -Known intolerance of clopidogrel or ASA -Long-term use of NSAIDs -Planned peri-procedural Tx with GP IIb/IIIa inhibitors -Known thrombocytopenia

Study	Regimens Evaluated	Outcomes Measured	Results	Limitations
PCI-CURE	Randomly assigned loading dose of clopidogrel or placebo, then aspirin+study drug until PCI, then 80% received open label thienopyridine+ASA for 2-4 weeks, then continued study drug for mean of 8 months	Primary Outcome (PO)= Composite of CV death, MI or urgent TVR w/in 30 days of PCI Secondary Outcome(SO)= CV death or MI from time of PCI to end of trial	30% relative risk reduction in primary end point w/loading dose clopidogrel 31% relative risk reduction in secondary outcome with maintenance dose copidogrel	-Limited to Pts with ACS -Observational study -Ignored role of GP IIb/IIIa -¼ received open label thienopyridine prior to PCI -Cannot truly separate PO from SO as early interventions are included in later results -External validity questionable
CREDO	Loading dose clopidogrel or placebo (randomly assigned) +ASA 3-24hrs prior to PCI, then all received clopidogrel + ASA for 28 days, then study drug or placebo from day 29 to 12 months	28 Day Outcome= Composite of death, MI or urgent TVR in the per-protocol population 1 Year Outcome= Composite of death, MI and stroke in the intent to treat population	Loading dose: non-significant 18.5% relative risk reduction Subgroup (clopidogrel >6hr prior to PCI) had fewer "events" Long-term use: 26.9% relative risk reduction (RRR) in the 1 Year Outcome	-Limited to patients awaiting planned PCI -Relatively high proportion of pts (39%) D/C'd study drug prior to completion of 1 year therapy -Pts not rerandomized after 28 days of therapy->not able to totally separate pre-treatment from long-term treatment benefits
TARGET Subset	Patients were randomized to receive abciximab or tirofiban. Loading dose clopidogrel 2-6hrs prior to PCI (or immediately preceding if emergent PCI) given with ASA [pre-treatment group] vs. loading dose clopidogrel immediately following procedure, [post-treatment group] then clopidogrel + ASA	-30 Day Outcome=Composite of death, MI or urgent TVR -6 Month Outcome=Composite of death, MI or any TVR at 6 months -1 Year Outcome= mortality at 1 year	-36.9% RRR in composite end point in pretreatment group (6.6% vs. 10.4%) -Pretreatment associated w/reduction in 6 mo composite end point (14.6% vs. 19.8%) -Pretreatment associated w/sig mortality reduction from 1.7% to 3.6%	-Timing of clopidogrel admin. not randomized -Observational study -Duration of clopidogrel therapy prior to procedure was variable -93% of the patients were included in pre-treatment group

Study	Regimens Evaluated	Outcomes Measured	Results	Limitations
"CBRACE"	Clopidogrel group received 375mg of clopidogrel the day prior to scheduled PCI in addition to their chronic ASA 75mg daily. This group continued on clopidogrel 75mg daily for 1 month if stent implanted. Historical control group received no clopidogrel pre-treatment in addition to chronic ASA 75mg daily. If stent was placed a loading dose of clopidogrel was immediately given after the procedure and clopidogrel 75mg daily or ticlopidine 250mg BID was continued for 1 month.	Primary outcome: In hospital cardiac events including death, MI, urgent bypass surgery, urgent repeat PCI and the composite of death, MI and urgent revascularization.	Clopidogrel pre-treatment group had a lower rate of in-hospital adverse cardiac events including the composite endpoint of death, MI or urgent revascularization (4.8% vs. 8.2%) Relative risk reduction=41%	-Main limitation is non-randomized design -Control & study groups not concurrent, i.e., control group 14 months preceding study group -Study confined to in-hospital events
"LEC"	Patients undergoing elective stent implantation were randomized to receive either clopidogrel 3 days prior to PCI or standard post-procedural treatment	-Primary end point: Rise in troponin I or CK-MB serum levels at 6-8hrs and 16-24hrs after PCI -Secondary end points: Death, stroke, MI, CABG, repeat PCI, and subacute stent thrombosis at 1 & 6 months after PCI, and the composite end point of above at 6 months	-No significant difference between pretreated and non-pretreated patients in the post-procedural elevations of troponin I and CK-MP -No significant difference at 1 & 6 month follow up, nor in composite end point at 6 mo. (12% vs. 13%)	-Small sample size -Limited to stable patients undergoing elective stent implantation