**Table F-3. Study characteristics table for KQ 3 comparisons—postdischarge treatment for UA/NSTEMI**

| **Study** | **Study Details** | **Intervention (N)** | **Comparator (N)** | **Cointerventions** | **Timing****Outcomes Reported** | **Quality** |
| --- | --- | --- | --- | --- | --- | --- |
| Alexander, 2008108CRUSADE | Observational550 sites in U.S.Funding: IndustryTimeframe: 01/2001–12/2005Population100% NSTEMI27% PCITotal N: 93,045Median Age: 70 to 71Female: 42%Race: 79% White | Clopidogrel(N=35,880) | No clopidogrel(N=57,165) | 93% ASA39% UFH29% GPI | Timing: In-hospitalComposite(primary)Total mortalityNonfatal MIIndividualTotal mortalityNonfatal MIStrokeMajor bleedingTransfusion | Fair |
| Aronow, 2008109BRAVO | Observational690 sites in U.S., Canada, Europe, Asia, Australia/NZOther: 23 countriesFunding: IndustryTimeframe: 05/1999–06/2000PopulationN= 954 UA/NSTEMIN=465 STEMIN=347 Stable CADTotal N: 4,589Median Age: 62 to 63Female: 29%Race: White 93% | ASA <162mg/dayMaintenance dose: 100 mg(N=2,368) | ASA >162 mg/dayMaintenance dose: 325 mg(N=2,221) | Placebo/control | Timing: 1 yr (366 days)Composite(secondary)Total mortalityNonfatal MIStroke(secondary)Total mortalityNonfatal MIStrokeRevascularizationRehospitalizationIndividualTotal mortalityNonfatal MIAnemiaStrokeRehospitalizationRevascularizationMajor bleedingAny bleedingTransfusionIntracranial hemorrhage | Good |
| Banerjee, 2011110 | ObservationalNR sites in U.S.Funding: NRTimeframe: 01/2003–12/2008Population89% ACSTotal N: 23,200Mean Age: 64 to 65Female: 1.7%Race: Hispanic 4%, Black 6%, White 54%, Other 37% | No PPI(N=3,678) | PPI(N=867) | ClopidogrelAll patients received clopidogrel | Timing: 1 yr, 6 yrComposite(primary)Total mortalityNonfatal MIRevascularization (secondary)Total mortalityNonfatal MIIndividualTotal mortalityRevascularization | Good |
| Barada, 2008111 | ObservationalSingle site in AfricaFunding: NoneTimeframe: 09/2001–11/2005Population: NRTotal N: 1,023Mean Age: 63 to 64Female: 26%Race: NR | No PPI(N=705) | PPI(N=318) | Clopidogrel, ASA | Timing: In-hospitalIndividualUGI bleeding | Poor |
| Bernardi, 2007112RACS | RCT18 sites in S. AmericaFunding: NRTimeframe: 04/2002–08/2003Population15% STEMI72% ACSTotal N: 1,004Mean Age:60 to 61Female: 20%Race: NR | Dual therapyclopidogrel 30 days + ASA 300 mg loading, 75 mg maintenance(N=502) | Dual Therapy clopidogrel 180 days + ASA 300 mg loading, 75 mg maintenance(N=502) | GPIsASA dose varied by physician, 75–325mg/dGPI was administered to 17% of patients by physician preference (tirofiban 32%, eptifibatide 17%, abciximab 50%) homogeneous distribution between groups | Timing: 30 days, 6 moComposite(primary) Total mortalityNonfatal MIStroke (secondary) Total mortalityNonfatal MIStrokeRevascularizationIndividualTotal mortality | Fair |
| Bhatt, 2010113COGENT | RCT393 sites location NRFunding: IndustryTimeframe: Jan2008-Dec2008PopulationNRTotal N: 3,761Median Age: 69Female: 32%Race: NR | Omeprazole 20 mg(N=1,876)Duration: 12 mo | Placebo(N=1,885) | ASA 75-325 mgClopidogrel 75 mg | Timing: 6 moComposite:(primary)CV mortalityNonfatal MIStrokeRevascularizationIndividualUpper GI eventsOvert gastroduodenal or upper GI bleedingNonfatal MIRevascularizationStrokeTotal mortalityCV mortality | Good |
| Bhurke, 2012114 | ObservationalMultiple sites in U.S.Funding: GovernmentTimeframe: 1/2001-12/2008Population100% ACSTotal N: 5348Mean Age: 61Female: 30 %Race: NR | Clopidogrel + PPI (N=2674) | Clopidogrel (N=2674) | NR | Timing: 1 yrComposite(primary)Nonfatal MIStentsNon-stenting revascIntermediate coronary syndromeIndividualNonfatal MIStents | Fair |
| Bonde, 2010115 | ObservationalMultiple sites in EuropeTimeframe: 1/2000-12/2005Population100% ACSTotal N: 11,142Mean Age: 70Female: 40%Race: NR | Placebo | Clopidogrel | Concomitant pharmacotherapy (range in 4 groups Clopidogrel Y, N and HF Y, N)Beta-blockers (75.7-83.7%) p=0.89ACE inhibitors (59.3-38.9%) p=0.58Statins (62.7-82.3%) p=0.55Glucose lowering drugs (9.0-21.3%) p= 0.18Vitamin K antagonist (4.3-8.8%) p=0.40 | Timing: 2 yrIndividualTotal mortality | Fair |
| Buresly, 2005116 | ObservationalSingle site in CanadaFunding: GovernmentTimeframe: 01/1996–03/1996Population: NRTotal N: 21,443Median Age 74Female: 43%Race: NR | ASA(N=656)Warfarin(N=195) | ASA(N=34)ASA(N=20) | Warfarin, Thienopyridine | Timing: 2 yrComposite(primary)Major bleedingMinor bleeding | Good |
| Butler, 2009117 | Observational12 sites in Australia/NZFunding: NRTimeframe: 04/2004–03/2007PopulationN= 418 STEMIN=1,393 ACSTotal N: 2,980Mean Age: 64 to 69Female: 27%Race: NR | (1) DES with clopidogrel intended duration ≤3 mo(N=152)DES with clopidogrel intended duration 6 mo (N=495)(2) BMS with clopidogrel intended duration ≤3 mo(N=287)BMS with clopidogrel intended duration 6 mo(N=340) | DES with clopidogrel intended duration ≥12 mo (N=1,022)BMS with clopidogrel intended duration ≥12 mo(N=684) | ASA, GPIs | Timing; 1 yrComposite(primary)Total mortalityNonfatal MIRevascularizationIndividualTotal mortalityMajor bleedingNonfatal MIRevascularizationPropensity scoreEquality of survivalDischarged aliveCumulative hazard of MACE for DES patients | Fair |
| Charlot, 2010118 | ObservationalNR sites in EuropeFunding: Private foundationTimeframe: 2000–2006Population: NRTotal N: 56,406Mean Age: 68.5Female: 41%Race: NR | No PPI(N=22,815)PPI(N=8,889) | No PPI(N=17,949)PPI(N=6,753) | No clopidogrelClopidogrel | Timing: 1 yrComposite(primary)CV mortalityNonfatal MIStrokeIndividualTotal mortalityCV mortalityNonfatal MIStroke | Good |
| Charlot, 2011119 | ObservationalNR sites in EuropeFunding: Private FoundationTimeframe: 1997–2006PopulationN= 19,925 ACSTotal N: 49,452Mean Age: 64 to 73Female: 76%Race: NR | No PPI(N=15,619) | PPI(N=4,306) | ASA 75 mg once a days | Timing: 1 yrComposite(primary)CV mortalityStrokeRehospitalizationIndividualTotal mortalityCV mortalityNonfatal MIStroke | Good |
| Charlot, 2012120 | ObservationalMultiple sites in EuropeFunding: Private FoundationTimeframe: 2004-2009Population67% NSTEMI19% STEMITotal N: 29,268Mean Age: 67Female: 33%Race: NR | Clopidogrel up to 90 days | Clopidogrel > 90 days | Intervention: 78.3% of patients were on ASAComparator: 88.3% of patients on ASA | Timing: 3 mo, 6 mo, 9 mo, 1 yr, 15 moComposite(primary)Total mortalityNonfatal MI | Fair |
| Cheng, 2010121T-ACCORD Registry | Observational27 sites in AsiaFunding: NRTimeframe: 04/2004–12/2006PopulationN=905 UAN=426 NSTEMITotal N: 1,331Mean Age: 63 to 69Female: 30%Race: NR | ASA(N=225)3rd treatment arm: Clopidogrel(N=250) | Dual therapy(N=856) | GPIs | Timing: 1 yrIndividualSurvival rate | Good |
| Chitose, 2011122KICS | Observational16 sites in AsiaFunding: Private foundation Timeframe: 06/2008–03/2009PopulationN=621 ACSTotal N: 1,270Mean Age: 69 to 72Female:30 %Race: Asian 100% | PPI (N=171) | No PPI(N=450) | Clopidogrel, ASAASA 100 mg/daythienopyridine agent (75 mg/day clopidogrel or 200 mg/day ticlopidine) | Timing: 18 moComposite(primary)CV mortalityNonfatal MIStrokeIndividualCV mortalityNonfatal MIStrokeGI event | Good |
| Evanchan, 2010123 | ObservationalSingle site in U.S.Funding: NRTimeframe: 01/2003–01/2008Population: NRTotal N: 5,794Mean Age: 63 to 64Female: NRRace: NR | PPI(N=1,369) | No PPI(N=4,425) | Clopidogrel at discharge | Timing: 1 yrIndividualNonfatal MI | Good |
| Fosbol, 2012124 | Observational514 sites in U.S.Funding: Private foundation, IndustryTimeframe: 1/2003-12/2006Population100% UA/NSTEMITotal N: 7619Median Age: 80Female: 48%Race: NR | Aspirin (N=2213)ASA + clopidogrel (N=2841) | Warfarin (N=563)ASA + warfarin (N=1271)ASA + clopidogrel + warfarin (N=731) | NR | Timing: 30 days, 1 yrComposite(primary)Total mortalityNonfatal MIStroke (any kind)IndividualMajor bleeding | Fair |
| Gao, 2009125 | RCT2 sites in AsiaFunding: NRTimeframe: Jan/2003-Dec/2007Population: NRTotal N: 237Mean Age: 58Female: 47%Race: NR | Omeprazole 40 mg loading, 20 mg maintenance(N=114) | Placebo(N=123) | NR | Timing: 14 daysIndividualTotal mortalityUpper GI bleeding | Poor |
| Gaspar, 2010126 | ObservationalSingle site in EuropeFunding: NRTimeframe: 12/2004–03/2008Population65% UA/NSTEMI35% STEMITotal N: 876Mean Age: 61 to 65Female: 24%Race: NR | PPI(N=274) | No PPI(N=528) | Clopidogrel, ASA, GPIs | Timing: 6 moComposite(primary)Total mortalityNonfatal MIUAIndividualTotal mortality | Good |
| Goodman, 2012127PLATO | Observational43 sites in U.S., Canada, UK, Europe, S. America, C. America, Asia, Africa, Australia/NZFunding: IndustryTimeframe: 10/2006–07/2008PopulationN= 3111 UAN=7950 NSTEMIN=7023 STEMITotal N: 18,624Median Age: 62 to 63Female: 28%Race: Black 1%, Asian 6%, White 92% | PPI(N=6,538) | No PPI(N=12,062) | Clopidogrel (N=9291; 300-mg loading dose, 75-mg daily maintenance dose)Clopidogrel (N=9291; 300-mg loading dose, 75-mg daily maintenance dose)Ticagrelor (N=9333; 180-mg loading dose, 90-mg twice daily maintenance dose)Ticagrelor (N=9333; 180-mg loading dose, 90-mg twice daily maintenance dose) | Timing; 1 yrComposite(primary)CV mortalityNonfatal MIStroke(secondary)CV mortalityNonfatal MIIndividualTotal mortalityCV mortalityNonfatal MIMajor bleedingStent thrombosis | Good |
| Gupta, 2010128 | ObservationalSingle site in U.S.Funding: NRTimeframe: 01/2003–08/2004Population: NRTotal N: 315Mean Age: 62Female: NRRace: NR | PPI(N=72) | No PPI(N=243) | Clopidogrel 75 mg/day | Timing: 4 yrComposite(primary)Total mortalityNonfatal MITVFIndividualTotal mortalityTLRTVF | Fair |
| Gwon, 2012129 | RCT19 sites in AsiaFunding: Government, IndustryTimeframe: 6/2008-7/2009Population48% UA/NSTEMI3% STEMITotal N: 1443Mean Age: 62 to 63Female: 35%Race: NR | ASA + Clopidogrel (N=722)Duration: 6 mo | ASA + Clopidogrel (N=721)Duration: 12 mo | Unfractionated heparin was administered throughout the procedure to maintain an activated clotting time of 􏰇250 seconds. Administration of glycoprotein IIb/IIIa inhibitors was at the discretion of the operator. After the procedure, all patients were recommended to receive optimal pharmacological therapy, including statins, 􏰉-blockers, or angiotensin-converting enzyme inhibitors at the discretion of the responsible clinicians. Any P2Y12 receptor antagonist other than clopidogrel was not used. | Timing: 1 yrComposite(primary)Cardiovascular mortalityNonfatal MITVR(secondary)Total mortalityNonfatal MI(secondary)Total mortalityNonfatal MIStroke (any kind)Revascularization(secondary)Total mortalityNonfatal MIStroke (any kind)Stent thrombosisMajor bleedingIndividualTotal mortalityCardiovascular mortalityNonfatal MIRevascularizationStent thrombosisMajor bleeding | Good |
| Harjai, 2009130 | ObservationalSingle site in U.S.Funding: Entirely funded by the Guthrie Health FoundationTimeframe: 04/2001–12/2006Population16% NSTEMI15% STEMI35% ACSTotal N: 1,859Mean Age: 64Female: 31%Race: NR | ASA 81–325 mg/day + clopidogrel 75 mg/day>12 mo (whole cohort any stent)(N=918)ASA 81–325 mg/day + clopidogrel 75 mg/day ≤ 12 mo (whole cohort any stent)(N=941) | DES subset of ASA 81–325 mg/day + clopidogrel 75 mg/day>12 mo (whole cohort any stent)(N=1,024)DES subset of ASA 81–325 mg/day + clopidogrel 75 mg/day ≤ 12 mo (whole cohort any stent)(N=588) | Clopidogrel, ASA, GPIs | Timing: 1775 days, 1080 days, 1287 days, 1226 days, 1 yr, 2 yr, 3 yr, 4 yr, 5 yrComposite(primary )Total mortalityNonfatal MIIndividualStent thrombosis | Good |
| Harjai, 2011131GHOST | ObservationalSingle site in U.S.Funding: NRTimeframe: 07/2001–12/2007Population40% NSTEMITotal N: 2820Mean Age: 64 to 67Female: 31%Race: NR | ASAMaintenance dose: 81 mg/day(N=313) | ASAMaintenance dose: 162-325 mg/day(N=2,507) | ClopidogrelDischarge ASA dose | Timing: 1 yrComposite(primary)Total mortalityNonfatal MIIndividualMajor bleeding | Fair |
| Harjai, 2011132 | ObservationalNR sites in U.S.Funding: NRTimeframe: 07/2001–12/2007Population39% NSTEMITotal N: 2,653Mean Age: 64 to 66Female: 31%Race: NR | PPI(N=1,902) | No PPI(N=751) | ASA. | Timing: 6 moComposite(primary)Total mortalityNonfatal MIRevascularizationStent thrombosisIndividualTotal mortalityNonfatal MIRevascularizationStent thrombosisMajor bleeding | Good |
| Ho, 2007133 | Observational127 sites in U.S.Funding: GovernmentTimeframe: 10/2003–09/2004PopulationN= 68 UAN=1387 ACSTotal N: 1,455Mean Age: 64Female: 2%Race: White 54% | Patients discontinued clopidogrel(N=variable)Duration: ongoing | Patients continued clopidogrel(N=variable)Duration: patients discontinued | GPIs | Timing: 6 mo, 299 days, 1 yr, 18 mo, 538 daysComposite(secondary) Total mortalityRehospitalization for acute MIIndividualTotal mortalityRehospitalization for acute MINonfatal MI | Fair |
| Ho, 2009134 | Observational127 sites in U.S.Funding: GovernmentTimeframe: 10/2003–12/2006PopulationTotal N: 8,790Mean Age: 66 to 68Female: 1%Race: NR | PPI(N=5,244) | No PPI(N=2,961) | Clopidogrel, ASA | Timing: 18 moComposite(primary)Total mortalityRehospitalizationIndividualRehospitalizationRevascularizationTotal mortality | Good |
| Hsiao, 2011135 | ObservationalNR sites in AsiaFunding: Private FoundationTimeframe: 01/2001–12/2006PopulationN= 9753 ACSTotal N: 9,753Mean Age: 62 to 66Female: 23%Race: NR | PPI(N=622) | No PPI(N=9,131) | Clopidogrel, ASA | Timing: 6 moIndividualRehospitalization | Good |
| Jang, 2011136 | Observational5 sites in AsiaFunding: NRTimeframe: 01/2005–12/2005Population21% UA17% NSTEMI19% STEMI43% Stable CADTotal N: 362 Mean Age: 68Female: 32%Race: NR | Warfarin(N=84) | Placebo(N=278) | Clopidogrel, ASA | Timing: 3 yrComposite(primary)Total mortalityNonfatal MIRevascularization(secondary)Total mortalityNonfatal MIStrokeRevascularizationMajor bleedingMinor bleedingIndividualTotal mortalityNonfatal MIRevascularizationStent thrombosisMajor bleedingMinor bleedingStroke | Poor |
| Juurlink, 2009137 | ObservationalNR sites in CanadaFunding: Government, Private FoundationTimeframe: Apr 2002-Dec 2007Population: NRTotal N: 2791Median Age: 77Female: 46%Race: NR | Clopidogrel + nonfatal MI in 90 days(N=734) | Clopidogrel (N=2,057) | PPI (intervention 39%, comparator 36%) | Timing: 3 mo, 1 yrIndividualTotal mortalityNonfatal MI | Good |
| Karjalainen, 2007138 | Observational3 sites in EuropeFunding: Private foundationTimeframe: 2003–2004Population18% UA24% NSTEMI12% STEMITotal N: 478Mean Age: 70Female: 26%Race: NR | Warfarin(N=239) | Placebo(N=239) | Clopidogrel, ASA | Timing: Discharge, 1 yrComposite(primary)Total mortalityNonfatal MIRevascularizationStent thrombosis(secondary)StrokeMajor bleedingIndividualStrokeMajor bleedingTotal mortalityNonfatal MIRevascularizationStent thrombosis | Good |
| Konstantino, 2006139 | ObservationalNR sites in IsraelFunding: NRTimeframe: 2000–2004Population100% ACS42% NSTEMI56% STEMITotal N: 2737Mean Age: 61 to 64Female: 21%Race: NR | Dual therapyASA + ticlopidine/ clopidogrel(N=2,661) | Triple therapyASA, ticlopidine/clopidogrel +warfarin(N=76) | Clopidogrel, ASA | Timing: In-hospital, 30 days, 6 moIndividualNonfatal MIStrokeMajor bleedingRehospitalizationTotal mortality | Fair |
| Kreutz, 2010140 | ObservationalNR sites in EuropeFunding: NRTimeframe: 10/2005–09/2006Population: NRTotal N: 16,690Mean Age: 65 to 68Female: 31%Race: NR | PPI(N=6,828) | No PPI(N=9,862) | Clopidogrel 75 mg/day | Timing: 1 yrComposite(primary)CV mortalityNonfatal MIStrokeRehospitalizationIndividualStrokeNonfatal MIRevascularizationCV mortality | Good |
| Lamberts, 2013141 | ObservationalDenmark Funding: private foundationTimeframe: 1/2001–12/2009Population: MI 90%PCI 10%Total N: 12,165Mean Age: 75.6 ±10.3 Female: 29%Race: NR | DAPT (ASA + clopidogrel)(N=3,590) | TT (ASA + clopidogrel + oral anticoagulant)(N=1,896) | NR | Timing: 1 yrCompositeNonfatal MITotal mortalityIndividual Total mortalityStroke Major bleeding | Good |
| Lim, 2005142 | Observational94 sites in U.S., Canada, UK, Europe, S. America, Australia/NZFunding: IndustryTimeframe: NRPopulation:55% UA45% NSTEMITotal N: 6,239Mean Age: 67 to 68Female: 38%Race: NR | ASA(N=4,625) | ASA + clopidogrel(N=1,614) | NR | Timing: 6 moIndividualTotal mortalityRehospitalizationRevascularizationStroke | Fair |
| Lopes, 2010143 | ObservationalSetting: NRFunding: NRTimeframe: 1995–2003PopulationN= 917 NSTEMITotal N: 23,208 Median Age: 69Female: 32%Race: Black 4%, White 91%, Other 5% | Warfarin(N=124) | Placebo(N=793) | Clopidogrel, ASAASA 62.9%, clopidogrel 10.5%Clopidogrel, ASAASA 89.0%, clopidogrel 26.4% | Timing: In-hospital, 6 moComposite(primary)Total mortalityNonfatal MIIndividualMajor bleedingStroke | Good |
| Maegdefessel, 2008144 | ObservationalSingle site in EuropeFunding: NRTimeframe: 1999–2004Population40% UA32% NSTEMI14% STEMI14% Stable CADTotal N: 159Mean Age: 70.3Female: 28%Race: White 100% | Clopidogrel(N=103) | Clopidogrel(N=42) | ASA, Enoxaparin, Warfarin | Timing: 1.4 yrIndividualMajor bleedingNonfatal MIStrokeCV mortality | Fair |
| Mahaffey, 2011145Wallentin, 200982PLATO | RCT862 international sitesFunding: IndustryPopulation16.7% UA42.7% NSTEMI37.6% STEMI72% underwent early invasive strategy64% received PCITotal N: 18,624Median Age: 62Female:28%Race: 92% White, 6% Asian, 1% Black | Ticagrelor 180 mg loading dose, 90 mg twice daily (N=9,333)Duration: 277 days (median) | Clopidogrel 300 mg or 600 mg loading dose, 75 mg daily (N=9,291) Duration: 277 days (median) | ASA use (97%) during hospitalization was similar between groupsUFH (56%) and LMWH (51%) used during hospitalization was similar between groupsGPI use was similar between groups (26%) | Timing: 30 days, 1 yrComposite (primary)CV mortalityNonfatal MIStroke(secondary) Total mortalityNonfatal MIStroke(secondary) CV mortalityNonfatal MIStrokeRecurrent ischemiaOther arterial thrombotic eventIndividualTotal mortalityCV mortalityNonfatal MIStrokeStent ThrombosisMajor BleedingMinor BleedingAdverse drug reactions | Good |
| Ng, 2008146 | Observational38 sites in AsiaFunding: NoneTimeframe: 01/2002–12/2006PopulationN= 375 UATotal N: 666Mean Age: 72Female: NRRace: NR | PPI(N=336) | No PPI(N=290) | Clopidogrel, ASA, enoxaparin | Timing: 7 daysIndividualGI bleedingGI bleeding/occult bleed | Good |
| Ng, 2011147 | RCTSingle site in AsiaFunding: Private FoundationTimeframe: Jul 2008-Sep 2010PopulationNRTotal N: 311Mean Age: 63 to 64Female: 25%Race: NR | Esomeprazole 20 mg(N=163)Duration: 16 wk | Famotidine 40 mg(N=148)Duration: 16 wk | ASA 80-160 mgClopidogrel 75 mg | Timing: 4 moComposite(secondary)CV mortalityNonfatal MIStroke(secondary)GI eventsOccult bleeding of unknown originIndividualGI events | Good |
| Nguyen, 2007148GRACE | Observational113 sites in U.S., Europe, S. America, Australia/NZFunding: IndustryTimeframe: 04/1999–09/2006Population16% UA23% NSTEMI61% STEMITotal N: 800Median Age: 64 to 66Female: 30%Race: NR | Triple therapyASA + thienopyridine(N=580) | Dual therapyASA or thienopyridine(N=220) | Warfarin | Timing: In-hospital, 6 moIndividualNonfatal MIStrokeCHFMajor bleedingTotal mortalityRevascularization | Good |
| O’Donoghue, 2009149TRITON-TIMI 38\* Substudy of Wiviott, 200784 | Observational707 international sitesFunding: IndustryPopulation74% UA/NSTEMI26% STEMITotal N: 13,608Median Age: 61Female: 26%Race: 93% White | Treated with a PPIPrasugrel 60 mg loading dose, 10 mg daily(N=2272)Clopidogrel 300 mg loading dose, 75 mg daily(N=2257)Duration: 14.5 mo (median) | Not treated with a PPIPrasugrel 60 mg loading dose, 10 mg daily(N=4541)Clopidogrel 300 mg loading dose, 75 mg daily(N=4538)Duration: 14.5 mo (median) | ASA daily dose 75–162 mg daily3% of patients received bivalirudin55% of patients received GPIs | Timing: 3 mo, 6 moComposite (primary)CV mortalityNonfatal MIStroke(secondary)Major bleedingMinor bleeding(secondary)MortalityMIStrokeMajor bleedingIndividualTotal mortalityCV mortalityNonfatal MIStent thrombosisMajor bleeding | Good |
| Ortolani, 2011150 | ObservationalNR sites in EuropeFunding: Private foundationTimeframe: 01/2008–08/2008PopulationN= 1141 UAN=1377 NSTEMIN=1378 STEMITotal N: 3,896Mean Age: 63 to 69Female: 30%Race: NR | PPI(N=3,519) | No PPI(N=377) | Clopidogrel, ASA | Timing: 1 yrComposite(secondary)Total mortalityRevascularizationRehospitalizationIndividualRehospitalizationRevascularizationTotal mortality | Good |
| Pekdemir, 2003151 | RCTSingle site in TurkeyFunding: NRTimeframe: 06/2000–12/2001PopulationN= 84 UAN=36 ACSN=110 Stable CADTotal N: 278Mean Age: 55 to 58Female: 43%Race: NR | Dual therapy1 mo ASA 100 mg/d + clopidogrel 75 mg/d(N=140)Duration: 1 mo | Dual therapy6 mo ASA 100 mg/d + clopidogrel 75 mg/d(N=138)Duration: 6 mo | Clopidogrel, ASA, tirofiban | Timing: 6 moComposite(primary) Total mortalityNonfatal MIRevascularizationIndividualMajor bleedingTotal mortalityNonfatal MIRevascularizationCABGRe-PTCASubacute stent occlusionLate stent occlusion | Fair |
| Persson, 2011152RIKS-HIA and SCAAR | Observational20 sites in EuropeFunding: Government, Private foundationTimeframe: 1997–2005Population79% UA/NSTEMI12% STEMI8% Stable CADTotal N: 27,972Median Age: 56 to 59Female: 28%Race: NR | Warfarin(N=1,183) | Placebo(N=26,789) | Clopidogrel, ASA, unfractionated heparin, low molecular weight heparins | Timing: 1 yrComposite(primary)Total mortalityNonfatal MIIndividualTotal mortalityStrokeMajor bleedingAny bleeding | Good |
| Peters, 2003153Yusuf, 2001154CURE | RCT482 sites in U.S., Canada, UK, Europe, S. America, C. America, Africa, Australia/NZFunding: IndustryTimeframe: D12/1998–09/2000PopulationN= 9414 UAN=3148 NSTEMITotal N: 12,562Mean Age: 64Female: 38%Race: NR | ClopidogrelLoading dose: 300 mgMaintenance dose: 75 mg daily(N=6,259) | PlaceboLoading dose: 300 mgMaintenance dose: 75 mg daily(N=6,303) | ASA, unfractionated heparin, GPIs, low molecular weight heparinsASA (75 to 325mg) daily. Patients in each group were to receive open label thienopyridine following PCI | Timing: 9 moComposite(primary)CV mortalityNonfatal MIStroke(primary)CV mortalityNonfatal MIStrokeRefractory ischemiaIndividualCV mortalityNonfatal MIStrokeRefractory ischemiaHeart failureSevere ischemiaRevascularizationMajor bleedingMinor bleeding | Good |
| Quinn, 2004155Gusto IIb and PURSUIT | Observational373 + 726 sites in U.S., Canada, UK,Europe, Australia/NZFunding: NR,Other: Original studies, both supported by industryTimeframe: 11/1995–01/1997 (PURSUIT) and 05/1994-10/1995 (GUSTO IIb)Population: NRTotal N: 20,469Median Age: 63 to 65Female: 32%Race: White 91% | ASAMaintenance dose: <150mg(N=6,128) | ASAMaintenance dose: =>150mg(N=14,341) | Eptifibatide, Unfractionated heparin, hirudin | Timing: 6 moComposite(primary)Total mortalityNonfatal MIStrokeIndividualTotal mortalityNonfatal MIStroke | Good |
| Rassen, 2009156 | ObservationalNR sites in U.S., CanadaFunding: GovernmentTimeframe: 01/2001–12/2005Population: NRTotal N: 18,565Mean Age: NRFemale: 20%Race: NR | PPI(N=3,996) | No PPI(N=14,569) | Clopidogrel | Timing: 6 moComposite(primary)Total mortalityNonfatal MIIndividualNonfatal MITotal mortalityRevascularization | Good |
| Ray, 2010157 | ObservationalNR sites in U.S.Funding: GovernmentTimeframe: 01/1999–12/2005Population: NRTotal N: 20,596Mean Age: 60 to 61Female: 50%Race: White 78% | No PPI(N=13,003) | PPI(N=7,593) | Clopidogrel | Timing: 1 yrComposite(primary)Total mortalityCV mortalityNonfatal MIStroke(secondary) Nonfatal MICV mortalityIndividualCV mortalityStrokeGastroduodenal bleedingOther bleeding | Good |
| Ren, 2011158 | RCTSingle site in AsiaFunding: NRTimeframe: NRPopulation: 100% ACSTotal N: 168Mean Age: 62Female: 28%Race: White NR | Omeprazole 20 mg(N=86)Duration: 30 days | Placebo(N=82) | ASA 100 mgClopidogrel 75 mg | Timing: 30 daysIndividualSlight chest pressureOccasional anginaTIAMajor bleeding | Poor |
| Rossini, 2008159 | Observational3 sites in EuropeFunding: NRTimeframe: 10/2005–08/2006Population45% UA/NSTEMI34% STEMI21% Stable CADTotal N: 204Mean Age: 68Female: 20%Race: NR  | Triple therapy(N=102) | Dual therapy(N=102) | Clopidogrel 300 mg loading dose/75 mg/day, ASA 100 mg/day, warfarin | Timing: 30 days,18 moComposite(primary)Major bleedingMinor bleeding(secondary)Total mortalityNonfatal MIStrokeIndividualMajor bleedingMinor bleeding | Good |
| Rossini, 2011160 | Observational2 sites in EuropeFunding: NRTimeframe: NRPopulation18% UA22% NSTEMI29% STEMI31% Stable CADTotal N: 1346Mean Age: 63 to 64Female: 24%Race: NR | PPI(N=1,158) | No PPI(N=170) | ASA 100 mg/day, clopidogrel 75 mg/day, GPIs | Timing: 1 yrCompositeTotal mortalityNonfatal MIStrokeRehospitalizationIndividualMajor bleedingMinor bleedingTotal mortalityStent thrombosis | Good |
| Roy, 2009161 | ObservationalSingle site in U.S.Funding: NRTimeframe: 04/2003–01/2007PopulationN=1,331 UATotal N: 2889Mean Age: 63 to 65Female: 34%Race: NR | Patients discontinued clopidogrel(N=61) | Patients continued clopidogrel(N=2,828) | ASA 325 mg, bivalirudin (bolus of 0.75 mg/kg, followed by an intravenous infusion of 1.75 mg/kg/hr) or unfractionated heparin (bolus of 40 U/kg and additional heparin to achieve an activated clotting time of 250 to 300 seconds), platelet GPIs  | Timing: 30 days, 6 mo, 1 yrIndividualStent thrombosis | Poor |
| Ruiz-Nodar, 2008162 | Observational2 sites in EuropeFunding: NRTimeframe: 01/2001–12/2006Population64% NSTEMI20% STEMI16% Stable CADTotal N: 426Mean Age: 71Female: 30%Race: NR | Warfarin(N=242) | ASA(N=184) | Clopidogrel, ASAwarfarin + ASA+ clopidogrel (N= 213), coumarin +ASA (N=8), coumarin + clopidogrel (N=16), coumarin N=5 | Timing: 5 yrComposite(primary)Total mortalityNonfatal MIRevascularization(secondary)StrokeMajor bleedingMACEIndividualTotal mortalityNonfatal MIRevascularizationMajor bleedingMinor bleeding | Good |
| Ruiz-Nodar, 2012163 | ObservationalNR sites in EuropeFunding: NRTimeframe: 1/2001-3/2008Population63% NSTEMI23% STEMITotal N: 590Mean age: 72Female: 28.8%Race: NR | Warfarin | Non-OAC | clopidogrel 94% of the total populationASA 89.6% of total populationwarfarin 56.3% of total populationwarfarin +ASA+clop 44.6% | Timing: 1 yrComposite(secondary)Total mortalityNonfatal MItarget vessel failureIndividualTotal mortalityMajor bleeding | Fair |
| Sarafoff, 2010164 | Observational2 sites in EuropeFunding: NRTimeframe: 07/2002–12/2006PopulationN= 781 UAN=2208 Stable CADTotal N: 3408 Mean Age: 66 to 69Female: 24%Race: NR | PPI(N=698) | No PPI(N=2,640) | Clopidogrel, ASAClopidogrel 75 mg twice daily together with ASA 100 mg twice daily | Timing: 30 daysComposite(secondary)Nonfatal MIStent thrombosisIndividualStent thrombosisTotal mortalityNonfatal MIMajor bleeding | Good |
| Schmidt, 2012165 | ObservationalNR sites in EuropeFunding: Private FoundationTimeframe: 01/2002-06/2005Population30.7% UATotal N: 13,001Mean Age: NRFemale: 28%Race: NR | PPI(N=2742) | No PPI(N=10,259) | Clopidogrel75 mg maintenance dose | Timing: In-hospitalComposite(primary)CV mortalityNonfatal MIStrokeStent ThrombosisTarget lesion revascularizationIndividualCV mortalityNonfatal MITarget lesion revascularization | Poor |
| Schulz, 2009166 | Observational2 sites in EuropeFunding: "No industry involvement" but does not specify source of fundsTimeframe: 07/2002–12/2006PopulationN= 1197 UAN=561 NSTEMIN=627 STEMIN=1188 ACSN=4431 Stable CADTotal N: 6,816Mean Age: 67Female: 24%Race: NR | Clopidogrel + ASALoading dose: 600 mg clopidogrel + 500 mg ASAMaintenance dose: 75mg clopidogrel daily + ASA 100 mg twice daily(N=6,816) | None | Bivalirudin, abciximab, unfractionated heparin | Timing: 29 days, 181 days, 30 days, 6 mo, 1 yr, 2 yr, 3 yr, 4 yrIndividualStent thrombosisHazard reduction per 1 days treatment continuationRisk of stent thrombosis within 4 yr | Fair |
| Sibbald, 2010167 | Observational247 sites location NRFunding: IndustryTimeframe: 04/1999–2007Population30% UA34% NSTEMI36% STEMITotal N: 44,426Median Age: 69 to 72Female: 33%Race: NR | Nonsmoker + no early clopidogrelIn-hospital(N=15,110)Nonsmoker + early clopidogrelIn-hospital(N=17,167) | Smoker + no early clopidogrelIn-hospital(N=4,791)Smoker + early clopidogrelIn-hospital(N=7,358) | ASA, unfractionated heparin, fibrinolytics, GPIsASA, enoxaparin, unfractionated heparin, fibrinolytics, GPIs | Timing: In-hospitalComposite(primary)Total mortalityNonfatal MI | Good |
| Simon, 2011168FAST-MI | Observational223 sites in EuropeFunding: Private Foundation, IndustryTimeframe: 10/2005–11/2005PopulationNSTEMI: % unreportedSTEMI: % unreportedUA: 0%Total N: 2744Mean Age: 64 to 74Female: 29.8%Race: NR | Clopidogrel at 48 hrsNo PPI(N=900)PPI(N=1,453) | No clopidogrelNo PPI(N=233)PPI(N=158) | Clopidogrel | Timing: In-hospital, 1 yrCompositeTotal mortalityNonfatal MIStrokeIndividualTotal mortalityNonfatal MIStrokeMajor bleeding | Good |
| So, 2009169 | ObservationalSingle site in CanadaFunding: NRTimeframe: 12/2003–11/2004Population52% UA/NSTEMI\25% STEMI19% Stable CADTotal N: 1,840Mean Age: 61 to 64Female: 27%Race: NR | ASA 81 mg/dMaintenance dose: 81mg/d(N=910) | ASA 325mg/dMaintenance dose: 325mg/d(N=930) | On clopidogrel n=906 (99.56%), on coumadin n= 84 (9.23%)On clopidogrel n=922 (99.14%), on coumadin n= 28 (3.01%) | Timing: 1 yrComposite(primary)Total mortalityNonfatal MI(secondary)Total mortalityNonfatal MIRevascularizationIndividualTotal mortalityRevascularization | Fair |
| Steinhubl, 2002170CREDO | RCT99 sites in U.S., CanadaFunding: IndustryTimeframe: 06/1999–04/2001Population53% UA14% NSTEMI33% Stable CADTotal N: 2,116Mean Age: 62Female: 29%Race: White 89% | Clopidogrel 300 or 600 mg loading dose, 75 mg maintenance dose(N=1,053) | Placebo loading dose, clopidogrel 75 mg maintenance dose(N=1,063) | ASA 325 mg loading dose/325 mg/d, clopidogrel 300 mg loading dose/75 mg/d  | Timing: 1 yrComposite(primary) Total mortalityNonfatal MIStrokeIndividualMajor bleeding | Good |
| Stenestrand, 2005171RIKS-HIA | Observational38 sites in EuropeFunding: Government, Private foundationTimeframe: 1995–2002Population29% STEMITotal N: 6275Mean Age: 75 to 79Female: 38%Race: NR | ASA(N=3,768) | OAC(N=1,848) | ThienopyridineASA and/or thienopyridine | Timing: 30 days, 1 yrIndividualTotal mortality | Good |
| Stockl, 2010172 | ObservationalNR sites in U.S.Funding: NRTimeframe: 01/2004–12/2006Population: NRTotal N: 2,066Mean Age: 69Female: 44%Race: NR | PPI(N=1,033) | No PPI(N=1,033) | Clopidogrel | Timing: 1 yrIndividualRehospitalization | Good |
| Tentzeris, 2010173 | ObservationalSingle site in EuropeFunding: Private foundationTimeframe: 01/2003–12/2006Population45% ACSTotal N: 1,210Mean Age: 64Female: 31%Race: NR | PPI(N=691) | No PPI(N=519) | Clopidogrel, ASAASA (100 mg/day after a loading dose of 250 mg IV), clopidogrel (75 mg/day after a loading dose of 300 mg or 600 mg) | Timing: 1 yrCompositeTotal mortalityRehospitalizationStent thrombosisIndividualTotal mortalityCV mortalityRehospitalizationStent thrombosis | Good |
| Tsai, 2011174 | ObservationalNR sites in AsiaFunding: NRTimeframe: Jan 2001-Dec 2006Population: NRTotal N: 3,580Mean Age: 71Female: 38%Race: NR | Clopidogrel + PPI(N=1,052)3rd treatment arm: ASA + PPI(N=1,203) | Clopidogrel(N=1,325) | NR | Timing: 1 yrComposite(primary)Nonfatal MIStrokeRehospitalizationIndividualGI events | Good |
| Valgimigli, 2012175PRODIGY | RCT3 sites in EuropeFunding: Private FoundationTimeframe: 12/2006–12/2008PopulationN= 365 UAN=450 NSTEMIN=648 STEMIN=507 Stable CADTotal N: 2013Mean Age: 68Female: 23%Race: NR | Clopidogrel 300 or 600 mg loading dose, 75 mg maintenance dose(N=987)Duration: 24 mo | Clopidogrel 300 or 600 mg loading dose, clopidogrel 75 mg maintenance dose(N=983)Duration: 6 mo | ASA 160–325 mg orally or 500 mg IV as a loading dose and then 80–160 mg orally indefinitely | Timing: 2 yrComposite(primary) Total mortalityNonfatal MIStroke(secondary) Total mortalityNonfatal MI(secondary)Total mortalityStrokeIndividualTotal mortalityCV mortalityStrokeStent thrombosisMinor bleeding | Good |
| Valkhoff, 2011176 | ObservationalSingle site in EuropeFunding: Private foundationTimeframe: 01/1999–12/2008Population: NRTotal N: 23,655 Mean Age: 65Female: 33%Race: NR | PPI(N=NR) | No PPI(N=NR) | Clopidogrel | Timing: 1 yrIndividualNonfatal MI | Poor |
| Van Boxel, 2010177 | ObservationalMultiple sites in EuropeFunding: IndustryTimeframe: Jan 2006-Dec 2007Population: NSTEMI % unknownSTEMI % unknownTotal N: 18,139Mean Age: 66 to 69Female: 36%Race: NR | Clopidogrel + PPI(N=5,734) | Clopidogrel(N=12,405) | NR | Timing: 30 days, 1 yrComposite(primary)Total mortalityNonfatal MIStrokeUAIndividualNonfatal MIUAStrokeTotal mortalityPeptic ulcer disease | Fair |
| Wu, 2010178 | ObservationalNR sites in AsiaFunding: GovernmentTimeframe: 07/2002–06/2005PopulationN= 5862 ACSTotal N: 6,300Mean Age: 66Female: NRRace: NR | PPI(N=311) | No PPI(N=5,551) | Clopidogrel | Timing: 3 moComposite(primary)Total mortalityRehospitalizationIndividualRehospitalizationRevascularizationTotal mortality | Good |
| Yusuf, 2001154CURE | RCT482 sites in U.S., Canada, UK, Europe, S. America, C. America, Africa, Australia/NZFunding: IndustryTimeframe: 12/1998–09/2000PopulationN= 9414 UAN=3148 NSTEMITotal N: 12,562Mean Age: 64Female: 38%Race: NR | ClopidogrelLoading dose: 300 mgMaintenance dose: 75 mg daily(N=6,259) | PlaceboLoading dose: 300 mgMaintenance dose: 75 mg daily(N=6,303) | ASA, unfractionated heparin, GPIs, low molecular weight heparinsASA (75 to 325mg) daily. Patients in each group were to receive open label thienopyridine following PCI | Timing: 9 moComposite(primary)CV mortalityNonfatal MIStroke(primary)CV mortalityNonfatal MIStrokeRefractory ischemiaIndividualCV mortalityNonfatal MIStrokeRefractory ischemiaHeart failureSevere ischemiaRevascularizationMajor bleedingMinor bleeding | Good |
| Zairis, 2010179 | ObservationalSingle site in EuropeFunding: NRTimeframe: Apr 2003-Jan 2005Population37% STEMI23% Stable angina40% UA/NSTEMITotal N: 588Mean Age: 62Female: 18%Race: NR | Omeprazole(N=340) | No PPI(N=248) | ASA 100-325 mgClopidogrel 75 mg | Timing: 1 yrComposite(primary)CV mortalityRehospitalizationIndividualRehospitalizationCV mortalityStent thrombosisRevascularization | Good |
| Zeymer, 2008180ACOS Registry | Observational155 sites in EuropeFunding: NRTimeframe: 06/2000–12/2002Population100% NSTEMI42% PCITotal N: 4,290Median Age: 67 to 72Female: 27%Race: NR | ASA + clopidogrel(N=2119) | ASA(N=2171) | NR | Timing: In-hospital, 1 yr Composite(primary)Total mortalityNonfatal MINonfatal strokeIndividualTotal mortalityNonfatal MIStroke | Poor |

Abbreviations: ACE=angiotensin converting enzyme; ACS=acute coronary syndrome; ASA=aspirin; BMS=bare metal stent; CABG=coronary artery bypass graft; CAD=coronary artery disease; CHF=congestive heart failure; CV=cardiovascular; d=day/days; DES=drug-eluting stent; GI=gastrointestinal; GPI=glycoprotein IIb/IIIa inhibitor; IV=intravenous; LMWH=low molecular weight heparin; MACE=major adverse cardiac event; mg=milligram/milligrams; MI=myocardial infarction; mo=month/months; N=number of patients; NR=not reported; NSTEMI=non-ST elevation myocardial infarction; NZ=New Zealand; OAC=oral anticoagulation; PCI=percutaneous coronary intervention; PPI=proton pump inhibitor; PTCA=percutaneous transluminal coronary angioplasty; RCT=randomized controlled trial; STEMI=ST elevation myocardial infarction; TIA=transient ischemic attack; TLR=target lesion revascularization; TVF=target vessel failure; U=unit/units; UA=unstable angina; UA/NSTEMI=unstable angina/non-ST elevation myocardial infarction; UFH=unfractionated heparin; UGI=upper gastrointestinal; UK=United Kingdom; U.S./US=United States; wk=week/weeks; yr=year/years