**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, 2008108  CRUSADE | Observational  550 sites in U.S.  Funding: Industry  Timeframe: 01/2001–12/2005  Population  100% NSTEMI  27% PCI  Total N: 93,045  Median Age: 70 to 71  Female: 42%  Race: 79% White | Clopidogrel  (N=35,880) | No clopidogrel  (N=57,165) | 93% ASA  39% UFH  29% GPI | Timing: In-hospital  Composite  (primary)  Total mortality  Nonfatal MI  Individual  Total mortality  Nonfatal MI  Stroke  Major bleeding  Transfusion | Fair |
| Aronow, 2008109  BRAVO | Observational  690 sites in U.S., Canada, Europe, Asia, Australia/NZ  Other: 23 countries  Funding: Industry  Timeframe: 05/1999–06/2000  Population  N= 954 UA/NSTEMI  N=465 STEMI  N=347 Stable CAD  Total N: 4,589  Median Age: 62 to 63  Female: 29%  Race: White 93% | ASA <162mg/day  Maintenance dose: 100 mg  (N=2,368) | ASA >162 mg/day  Maintenance dose: 325 mg  (N=2,221) | Placebo/control | Timing: 1 yr (366 days)  Composite  (secondary)  Total mortality  Nonfatal MI  Stroke  (secondary)  Total mortality  Nonfatal MI  Stroke  Revascularization  Rehospitalization  Individual  Total mortality  Nonfatal MI  Anemia  Stroke  Rehospitalization  Revascularization  Major bleeding  Any bleeding  Transfusion  Intracranial hemorrhage | Good |
| Banerjee, 2011110 | Observational  NR sites in U.S.  Funding: NR  Timeframe: 01/2003–12/2008  Population  89% ACS  Total N: 23,200  Mean Age: 64 to 65  Female: 1.7%  Race: Hispanic 4%, Black 6%, White 54%, Other 37% | No PPI  (N=3,678) | PPI  (N=867) | Clopidogrel  All patients received clopidogrel | Timing: 1 yr, 6 yr  Composite  (primary)  Total mortality  Nonfatal MI  Revascularization    (secondary)  Total mortality  Nonfatal MI  Individual  Total mortality  Revascularization | Good |
| Barada, 2008111 | Observational  Single site in Africa  Funding: None  Timeframe: 09/2001–11/2005  Population:  NR  Total N: 1,023  Mean Age: 63 to 64  Female: 26%  Race: NR | No PPI  (N=705) | PPI  (N=318) | Clopidogrel, ASA | Timing: In-hospital  Individual  UGI bleeding | Poor |
| Bernardi, 2007112  RACS | RCT  18 sites in S. America  Funding: NR  Timeframe: 04/2002–08/2003  Population  15% STEMI  72% ACS  Total N: 1,004  Mean Age:60 to 61  Female: 20%  Race: NR | Dual therapy  clopidogrel 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) | GPIs  ASA dose varied by physician, 75–325mg/d  GPI was administered to 17% of patients by physician preference (tirofiban 32%, eptifibatide 17%, abciximab 50%) homogeneous distribution between groups | Timing: 30 days, 6 mo  Composite  (primary)  Total mortality  Nonfatal MI  Stroke    (secondary)  Total mortality  Nonfatal MI  Stroke  Revascularization  Individual  Total mortality | Fair |
| Bhatt, 2010113  COGENT | RCT  393 sites location NR  Funding: Industry  Timeframe: Jan2008-Dec2008  Population  NR  Total N: 3,761  Median Age: 69  Female: 32%  Race: NR | Omeprazole 20 mg  (N=1,876)  Duration: 12 mo | Placebo  (N=1,885) | ASA 75-325 mg  Clopidogrel 75 mg | Timing: 6 mo  Composite:  (primary)  CV mortality  Nonfatal MI  Stroke  Revascularization  Individual  Upper GI events  Overt gastroduodenal or upper GI bleeding  Nonfatal MI  Revascularization  Stroke  Total mortality  CV mortality | Good |
| Bhurke, 2012114 | Observational  Multiple sites in U.S.  Funding: Government  Timeframe: 1/2001-12/2008  Population  100% ACS  Total N: 5348  Mean Age: 61  Female: 30 %  Race: NR | Clopidogrel + PPI (N=2674) | Clopidogrel (N=2674) | NR | Timing: 1 yr  Composite  (primary)  Nonfatal MI  Stents  Non-stenting revasc  Intermediate coronary syndrome  Individual  Nonfatal MI  Stents | Fair |
| Bonde, 2010115 | Observational  Multiple sites in Europe  Timeframe: 1/2000-12/2005  Population  100% ACS  Total N: 11,142  Mean Age: 70  Female: 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=0.89  ACE inhibitors (59.3-38.9%) p=0.58  Statins (62.7-82.3%) p=0.55  Glucose lowering drugs (9.0-21.3%) p= 0.18  Vitamin K antagonist (4.3-8.8%) p=0.40 | Timing: 2 yr  Individual  Total mortality | Fair |
| Buresly, 2005116 | Observational  Single site in Canada  Funding: Government  Timeframe: 01/1996–03/1996  Population: NR  Total N: 21,443  Median Age 74  Female: 43%  Race: NR | ASA  (N=656)  Warfarin  (N=195) | ASA  (N=34)  ASA  (N=20) | Warfarin, Thienopyridine | Timing: 2 yr  Composite  (primary)  Major bleeding  Minor bleeding | Good |
| Butler, 2009117 | Observational  12 sites in Australia/NZ  Funding: NR  Timeframe: 04/2004–03/2007  Population  N= 418 STEMI  N=1,393 ACS  Total N: 2,980  Mean Age: 64 to 69  Female: 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 yr  Composite  (primary)  Total mortality  Nonfatal MI  Revascularization  Individual  Total mortality  Major bleeding  Nonfatal MI  Revascularization  Propensity score  Equality of survival  Discharged alive  Cumulative hazard of MACE for DES patients | Fair |
| Charlot, 2010118 | Observational  NR sites in Europe  Funding: Private foundation  Timeframe: 2000–2006  Population: NR  Total N: 56,406  Mean Age: 68.5  Female: 41%  Race: NR | No PPI  (N=22,815)  PPI  (N=8,889) | No PPI  (N=17,949)  PPI  (N=6,753) | No clopidogrel  Clopidogrel | Timing: 1 yr  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  Individual  Total mortality  CV mortality  Nonfatal MI  Stroke | Good |
| Charlot, 2011119 | Observational  NR sites in Europe  Funding: Private Foundation  Timeframe: 1997–2006  Population  N= 19,925 ACS  Total N: 49,452  Mean Age: 64 to 73  Female: 76%  Race: NR | No PPI  (N=15,619) | PPI  (N=4,306) | ASA 75 mg once a days | Timing: 1 yr  Composite  (primary)  CV mortality  Stroke  Rehospitalization  Individual  Total mortality  CV mortality  Nonfatal MI  Stroke | Good |
| Charlot, 2012120 | Observational  Multiple sites in Europe  Funding: Private Foundation  Timeframe: 2004-2009  Population  67% NSTEMI  19% STEMI  Total N: 29,268  Mean Age: 67  Female: 33%  Race: NR | Clopidogrel up to 90 days | Clopidogrel > 90 days | Intervention: 78.3% of patients were on ASA  Comparator: 88.3% of patients on ASA | Timing: 3 mo, 6 mo, 9 mo, 1 yr, 15 mo  Composite  (primary)  Total mortality  Nonfatal MI | Fair |
| Cheng, 2010121  T-ACCORD Registry | Observational  27 sites in Asia  Funding: NR  Timeframe: 04/2004–12/2006  Population  N=905 UA  N=426 NSTEMI  Total N: 1,331  Mean Age: 63 to 69  Female: 30%  Race: NR | ASA  (N=225)  3rd treatment arm: Clopidogrel  (N=250) | Dual therapy  (N=856) | GPIs | Timing: 1 yr  Individual  Survival rate | Good |
| Chitose, 2011122  KICS | Observational  16 sites in Asia  Funding: Private foundation  Timeframe: 06/2008–03/2009  Population  N=621 ACS  Total N: 1,270  Mean Age: 69 to 72  Female:30 %  Race: Asian 100% | PPI  (N=171) | No PPI  (N=450) | Clopidogrel, ASA  ASA 100 mg/day  thienopyridine agent (75 mg/day clopidogrel or 200 mg/day ticlopidine) | Timing: 18 mo  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  Individual  CV mortality  Nonfatal MI  Stroke  GI event | Good |
| Evanchan, 2010123 | Observational  Single site in U.S.  Funding: NR  Timeframe: 01/2003–01/2008  Population:  NR  Total N: 5,794  Mean Age: 63 to 64  Female: NR  Race: NR | PPI  (N=1,369) | No PPI  (N=4,425) | Clopidogrel at discharge | Timing: 1 yr  Individual  Nonfatal MI | Good |
| Fosbol, 2012124 | Observational  514 sites in U.S.  Funding: Private foundation, Industry  Timeframe: 1/2003-12/2006  Population  100% UA/NSTEMI  Total N: 7619  Median Age: 80  Female: 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 yr  Composite  (primary)  Total mortality  Nonfatal MI  Stroke (any kind)  Individual  Major bleeding | Fair |
| Gao, 2009125 | RCT  2 sites in Asia  Funding: NR  Timeframe: Jan/2003-Dec/2007  Population:  NR  Total N: 237  Mean Age: 58  Female: 47%  Race: NR | Omeprazole 40 mg loading, 20 mg maintenance  (N=114) | Placebo  (N=123) | NR | Timing: 14 days  Individual  Total mortality  Upper GI bleeding | Poor |
| Gaspar, 2010126 | Observational  Single site in Europe  Funding: NR  Timeframe: 12/2004–03/2008  Population  65% UA/NSTEMI  35% STEMI  Total N: 876  Mean Age: 61 to 65  Female: 24%  Race: NR | PPI  (N=274) | No PPI  (N=528) | Clopidogrel, ASA, GPIs | Timing: 6 mo  Composite  (primary)  Total mortality  Nonfatal MI  UA  Individual  Total mortality | Good |
| Goodman, 2012127  PLATO | Observational  43 sites in U.S., Canada, UK, Europe, S. America, C. America, Asia, Africa, Australia/NZ  Funding: Industry  Timeframe: 10/2006–07/2008  Population  N= 3111 UA  N=7950 NSTEMI  N=7023 STEMI  Total N: 18,624  Median Age: 62 to 63  Female: 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 yr  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  (secondary)  CV mortality  Nonfatal MI  Individual  Total mortality  CV mortality  Nonfatal MI  Major bleeding  Stent thrombosis | Good |
| Gupta, 2010128 | Observational  Single site in U.S.  Funding: NR  Timeframe: 01/2003–08/2004  Population:  NR  Total N: 315  Mean Age: 62  Female: NR  Race: NR | PPI  (N=72) | No PPI  (N=243) | Clopidogrel 75 mg/day | Timing: 4 yr  Composite  (primary)  Total mortality  Nonfatal MI  TVF  Individual  Total mortality  TLR  TVF | Fair |
| Gwon, 2012129 | RCT  19 sites in Asia  Funding: Government, Industry  Timeframe: 6/2008-7/2009  Population  48% UA/NSTEMI  3% STEMI  Total N: 1443  Mean Age: 62 to 63  Female: 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 yr  Composite  (primary)  Cardiovascular mortality  Nonfatal MI  TVR  (secondary)  Total mortality  Nonfatal MI  (secondary)  Total mortality  Nonfatal MI  Stroke (any kind)  Revascularization  (secondary)  Total mortality  Nonfatal MI  Stroke (any kind)  Stent thrombosis  Major bleeding  Individual  Total mortality  Cardiovascular mortality  Nonfatal MI  Revascularization  Stent thrombosis  Major bleeding | Good |
| Harjai, 2009130 | Observational  Single site in U.S.  Funding: Entirely funded by the Guthrie Health Foundation  Timeframe: 04/2001–12/2006  Population  16% NSTEMI  15% STEMI  35% ACS  Total N: 1,859  Mean Age: 64  Female: 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 yr  Composite  (primary )  Total mortality  Nonfatal MI  Individual  Stent thrombosis | Good |
| Harjai, 2011131  GHOST | Observational  Single site in U.S.  Funding: NR  Timeframe: 07/2001–12/2007  Population  40% NSTEMI  Total N: 2820  Mean Age: 64 to 67  Female: 31%  Race: NR | ASA  Maintenance dose: 81 mg/day  (N=313) | ASA  Maintenance dose: 162-325 mg/day  (N=2,507) | Clopidogrel  Discharge ASA dose | Timing: 1 yr  Composite  (primary)  Total mortality  Nonfatal MI  Individual  Major bleeding | Fair |
| Harjai, 2011132 | Observational  NR sites in U.S.  Funding: NR  Timeframe: 07/2001–12/2007  Population  39% NSTEMI  Total N: 2,653  Mean Age: 64 to 66  Female: 31%  Race: NR | PPI  (N=1,902) | No PPI  (N=751) | ASA. | Timing: 6 mo  Composite  (primary)  Total mortality  Nonfatal MI  Revascularization  Stent thrombosis  Individual  Total mortality  Nonfatal MI  Revascularization  Stent thrombosis  Major bleeding | Good |
| Ho, 2007133 | Observational  127 sites in U.S.  Funding: Government  Timeframe: 10/2003–09/2004  Population  N= 68 UA  N=1387 ACS  Total N: 1,455  Mean Age: 64  Female: 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 days  Composite  (secondary)  Total mortality  Rehospitalization for acute MI  Individual  Total mortality  Rehospitalization for acute MI  Nonfatal MI | Fair |
| Ho, 2009134 | Observational  127 sites in U.S.  Funding: Government  Timeframe: 10/2003–12/2006  Population  Total N: 8,790  Mean Age: 66 to 68  Female: 1%  Race: NR | PPI  (N=5,244) | No PPI  (N=2,961) | Clopidogrel, ASA | Timing: 18 mo  Composite  (primary)  Total mortality  Rehospitalization  Individual  Rehospitalization  Revascularization  Total mortality | Good |
| Hsiao, 2011135 | Observational  NR sites in Asia  Funding: Private Foundation  Timeframe: 01/2001–12/2006  Population  N= 9753 ACS  Total N: 9,753  Mean Age: 62 to 66  Female: 23%  Race: NR | PPI  (N=622) | No PPI  (N=9,131) | Clopidogrel, ASA | Timing: 6 mo  Individual  Rehospitalization | Good |
| Jang, 2011136 | Observational  5 sites in Asia  Funding: NR  Timeframe: 01/2005–12/2005  Population  21% UA  17% NSTEMI  19% STEMI  43% Stable CAD  Total N: 362  Mean Age: 68  Female: 32%  Race: NR | Warfarin  (N=84) | Placebo  (N=278) | Clopidogrel, ASA | Timing: 3 yr  Composite  (primary)  Total mortality  Nonfatal MI  Revascularization  (secondary)  Total mortality  Nonfatal MI  Stroke  Revascularization  Major bleeding  Minor bleeding  Individual  Total mortality  Nonfatal MI  Revascularization  Stent thrombosis  Major bleeding  Minor bleeding  Stroke | Poor |
| Juurlink, 2009137 | Observational  NR sites in Canada  Funding: Government, Private Foundation  Timeframe: Apr 2002-Dec 2007  Population:  NR  Total N: 2791  Median Age: 77  Female: 46%  Race: NR | Clopidogrel + nonfatal MI in 90 days  (N=734) | Clopidogrel  (N=2,057) | PPI (intervention 39%, comparator 36%) | Timing: 3 mo, 1 yr  Individual  Total mortality  Nonfatal MI | Good |
| Karjalainen, 2007138 | Observational  3 sites in Europe  Funding: Private foundation  Timeframe: 2003–2004  Population  18% UA  24% NSTEMI  12% STEMI  Total N: 478  Mean Age: 70  Female: 26%  Race: NR | Warfarin  (N=239) | Placebo  (N=239) | Clopidogrel, ASA | Timing: Discharge, 1 yr  Composite  (primary)  Total mortality  Nonfatal MI  Revascularization  Stent thrombosis  (secondary)  Stroke  Major bleeding  Individual  Stroke  Major bleeding  Total mortality  Nonfatal MI  Revascularization  Stent thrombosis | Good |
| Konstantino, 2006139 | Observational  NR sites in Israel  Funding: NR  Timeframe: 2000–2004  Population  100% ACS  42% NSTEMI  56% STEMI  Total N: 2737  Mean Age: 61 to 64  Female: 21%  Race: NR | Dual therapy  ASA + ticlopidine/ clopidogrel  (N=2,661) | Triple therapy  ASA, ticlopidine/clopidogrel +warfarin  (N=76) | Clopidogrel, ASA | Timing: In-hospital, 30 days, 6 mo  Individual  Nonfatal MI  Stroke  Major bleeding  Rehospitalization  Total mortality | Fair |
| Kreutz, 2010140 | Observational  NR sites in Europe  Funding: NR  Timeframe: 10/2005–09/2006  Population:  NR  Total N: 16,690  Mean Age: 65 to 68  Female: 31%  Race: NR | PPI  (N=6,828) | No PPI  (N=9,862) | Clopidogrel 75 mg/day | Timing: 1 yr  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  Rehospitalization  Individual  Stroke  Nonfatal MI  Revascularization  CV mortality | Good |
| Lamberts, 2013141 | Observational  Denmark  Funding: private foundation  Timeframe: 1/2001–12/2009  Population:  MI 90%  PCI 10%  Total N: 12,165  Mean 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 yr  Composite  Nonfatal MI  Total mortality  Individual  Total mortality  Stroke  Major bleeding | Good |
| Lim, 2005142 | Observational  94 sites in U.S., Canada, UK, Europe, S. America, Australia/NZ  Funding: Industry  Timeframe: NR  Population:  55% UA  45% NSTEMI  Total N: 6,239  Mean Age: 67 to 68  Female: 38%  Race: NR | ASA  (N=4,625) | ASA + clopidogrel  (N=1,614) | NR | Timing: 6 mo  Individual  Total mortality  Rehospitalization  Revascularization  Stroke | Fair |
| Lopes, 2010143 | Observational  Setting: NR  Funding: NR  Timeframe: 1995–2003  Population  N= 917 NSTEMI  Total N: 23,208  Median Age: 69  Female: 32%  Race: Black 4%, White 91%, Other 5% | Warfarin  (N=124) | Placebo  (N=793) | Clopidogrel, ASA  ASA 62.9%, clopidogrel 10.5%  Clopidogrel, ASA  ASA 89.0%, clopidogrel 26.4% | Timing: In-hospital, 6 mo  Composite  (primary)  Total mortality  Nonfatal MI  Individual  Major bleeding  Stroke | Good |
| Maegdefessel, 2008144 | Observational  Single site in Europe  Funding: NR  Timeframe: 1999–2004  Population  40% UA  32% NSTEMI  14% STEMI  14% Stable CAD  Total N: 159  Mean Age: 70.3  Female: 28%  Race: White 100% | Clopidogrel  (N=103) | Clopidogrel  (N=42) | ASA, Enoxaparin, Warfarin | Timing: 1.4 yr  Individual  Major bleeding  Nonfatal MI  Stroke  CV mortality | Fair |
| Mahaffey, 2011145  Wallentin, 200982  PLATO | RCT  862 international sites  Funding: Industry  Population  16.7% UA  42.7% NSTEMI  37.6% STEMI  72% underwent early invasive strategy  64% received PCI  Total N: 18,624  Median Age: 62  Female: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 groups  UFH (56%) and LMWH (51%) used during hospitalization was similar between groups  GPI use was similar between groups (26%) | Timing: 30 days, 1 yr  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  (secondary)  Total mortality  Nonfatal MI  Stroke  (secondary)  CV mortality  Nonfatal MI  Stroke  Recurrent ischemia  Other arterial thrombotic event  Individual  Total mortality  CV mortality  Nonfatal MI  Stroke  Stent Thrombosis  Major Bleeding  Minor Bleeding  Adverse drug reactions | Good |
| Ng, 2008146 | Observational  38 sites in Asia  Funding: None  Timeframe: 01/2002–12/2006  Population  N= 375 UA  Total N: 666  Mean Age: 72  Female: NR  Race: NR | PPI  (N=336) | No PPI  (N=290) | Clopidogrel, ASA, enoxaparin | Timing: 7 days  Individual  GI bleeding  GI bleeding/occult bleed | Good |
| Ng, 2011147 | RCT  Single site in Asia  Funding: Private Foundation  Timeframe: Jul 2008-Sep 2010  Population  NR  Total N: 311  Mean Age: 63 to 64  Female: 25%  Race: NR | Esomeprazole 20 mg  (N=163)  Duration: 16 wk | Famotidine 40 mg  (N=148)  Duration: 16 wk | ASA 80-160 mg  Clopidogrel 75 mg | Timing: 4 mo  Composite  (secondary)  CV mortality  Nonfatal MI  Stroke  (secondary)  GI events  Occult bleeding of unknown origin  Individual  GI events | Good |
| Nguyen, 2007148  GRACE | Observational  113 sites in U.S., Europe, S. America, Australia/NZ  Funding: Industry  Timeframe: 04/1999–09/2006  Population  16% UA  23% NSTEMI  61% STEMI  Total N: 800  Median Age: 64 to 66  Female: 30%  Race: NR | Triple therapy  ASA + thienopyridine  (N=580) | Dual therapy  ASA or thienopyridine  (N=220) | Warfarin | Timing: In-hospital, 6 mo  Individual  Nonfatal MI  Stroke  CHF  Major bleeding  Total mortality  Revascularization | Good |
| O’Donoghue, 2009149  TRITON-TIMI 38  \* Substudy of Wiviott, 200784 | Observational  707 international sites  Funding: Industry  Population  74% UA/NSTEMI  26% STEMI  Total N: 13,608  Median Age: 61  Female: 26%  Race: 93% White | Treated with a PPI  Prasugrel 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 PPI  Prasugrel 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 daily  3% of patients received bivalirudin  55% of patients received GPIs | Timing: 3 mo, 6 mo  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  (secondary)  Major bleeding  Minor bleeding  (secondary)  Mortality  MI  Stroke  Major bleeding  Individual  Total mortality  CV mortality  Nonfatal MI  Stent thrombosis  Major bleeding | Good |
| Ortolani, 2011150 | Observational  NR sites in Europe  Funding: Private foundation  Timeframe: 01/2008–08/2008  Population  N= 1141 UA  N=1377 NSTEMI  N=1378 STEMI  Total N: 3,896  Mean Age: 63 to 69  Female: 30%  Race: NR | PPI  (N=3,519) | No PPI  (N=377) | Clopidogrel, ASA | Timing: 1 yr  Composite  (secondary)  Total mortality  Revascularization  Rehospitalization  Individual  Rehospitalization  Revascularization  Total mortality | Good |
| Pekdemir, 2003151 | RCT  Single site in Turkey  Funding: NR  Timeframe: 06/2000–12/2001  Population  N= 84 UA  N=36 ACS  N=110 Stable CAD  Total N: 278  Mean Age: 55 to 58  Female: 43%  Race: NR | Dual therapy  1 mo ASA 100 mg/d + clopidogrel 75 mg/d  (N=140)  Duration: 1 mo | Dual therapy  6 mo ASA 100 mg/d + clopidogrel 75 mg/d  (N=138)  Duration: 6 mo | Clopidogrel, ASA, tirofiban | Timing: 6 mo  Composite  (primary)  Total mortality  Nonfatal MI  Revascularization  Individual  Major bleeding  Total mortality  Nonfatal MI  Revascularization  CABG  Re-PTCA  Subacute stent occlusion  Late stent occlusion | Fair |
| Persson, 2011152  RIKS-HIA and SCAAR | Observational  20 sites in Europe  Funding: Government, Private foundation  Timeframe: 1997–2005  Population  79% UA/NSTEMI  12% STEMI  8% Stable CAD  Total N: 27,972  Median Age: 56 to 59  Female: 28%  Race: NR | Warfarin  (N=1,183) | Placebo  (N=26,789) | Clopidogrel, ASA, unfractionated heparin, low molecular weight heparins | Timing: 1 yr  Composite  (primary)  Total mortality  Nonfatal MI  Individual  Total mortality  Stroke  Major bleeding  Any bleeding | Good |
| Peters, 2003153  Yusuf, 2001154  CURE | RCT  482 sites in U.S., Canada, UK, Europe, S. America, C. America, Africa, Australia/NZ  Funding: Industry  Timeframe: D12/1998–09/2000  Population  N= 9414 UA  N=3148 NSTEMI  Total N: 12,562  Mean Age: 64  Female: 38%  Race: NR | Clopidogrel  Loading dose: 300 mg  Maintenance dose: 75 mg daily  (N=6,259) | Placebo  Loading dose: 300 mg  Maintenance dose: 75 mg daily  (N=6,303) | ASA, unfractionated heparin, GPIs, low molecular weight heparins  ASA (75 to 325mg) daily. Patients in each group were to receive open label thienopyridine following PCI | Timing: 9 mo  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  (primary)  CV mortality  Nonfatal MI  Stroke  Refractory ischemia  Individual  CV mortality  Nonfatal MI  Stroke  Refractory ischemia  Heart failure  Severe ischemia  Revascularization  Major bleeding  Minor bleeding | Good |
| Quinn, 2004155  Gusto IIb and PURSUIT | Observational  373 + 726 sites in U.S., Canada, UK,  Europe, Australia/NZ  Funding: NR,  Other: Original studies, both supported by industry  Timeframe: 11/1995–01/1997 (PURSUIT) and 05/1994-10/1995 (GUSTO IIb)  Population: NR  Total N: 20,469  Median Age: 63 to 65  Female: 32%  Race: White 91% | ASA  Maintenance dose: <150mg  (N=6,128) | ASA  Maintenance dose: =>150mg  (N=14,341) | Eptifibatide, Unfractionated heparin, hirudin | Timing: 6 mo  Composite  (primary)  Total mortality  Nonfatal MI  Stroke  Individual  Total mortality  Nonfatal MI  Stroke | Good |
| Rassen, 2009156 | Observational  NR sites in U.S., Canada  Funding: Government  Timeframe: 01/2001–12/2005  Population:  NR  Total N: 18,565  Mean Age: NR  Female: 20%  Race: NR | PPI  (N=3,996) | No PPI  (N=14,569) | Clopidogrel | Timing: 6 mo  Composite  (primary)  Total mortality  Nonfatal MI  Individual  Nonfatal MI  Total mortality  Revascularization | Good |
| Ray, 2010157 | Observational  NR sites in U.S.  Funding: Government  Timeframe: 01/1999–12/2005  Population:  NR  Total N: 20,596  Mean Age: 60 to 61  Female: 50%  Race: White 78% | No PPI  (N=13,003) | PPI  (N=7,593) | Clopidogrel | Timing: 1 yr  Composite  (primary)  Total mortality  CV mortality  Nonfatal MI  Stroke  (secondary)  Nonfatal MI  CV mortality  Individual  CV mortality  Stroke  Gastroduodenal bleeding  Other bleeding | Good |
| Ren, 2011158 | RCT  Single site in Asia  Funding: NR  Timeframe: NR  Population:  100% ACS  Total N: 168  Mean Age: 62  Female: 28%  Race: White NR | Omeprazole 20 mg  (N=86)  Duration: 30 days | Placebo  (N=82) | ASA 100 mg  Clopidogrel 75 mg | Timing: 30 days  Individual  Slight chest pressure  Occasional angina  TIA  Major bleeding | Poor |
| Rossini, 2008159 | Observational  3 sites in Europe  Funding: NR  Timeframe: 10/2005–08/2006  Population  45% UA/NSTEMI  34% STEMI  21% Stable CAD  Total N: 204  Mean Age: 68  Female: 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 mo  Composite  (primary)  Major bleeding  Minor bleeding  (secondary)  Total mortality  Nonfatal MI  Stroke  Individual  Major bleeding  Minor bleeding | Good |
| Rossini, 2011160 | Observational  2 sites in Europe  Funding: NR  Timeframe: NR  Population  18% UA  22% NSTEMI  29% STEMI  31% Stable CAD  Total N: 1346  Mean Age: 63 to 64  Female: 24%  Race: NR | PPI  (N=1,158) | No PPI  (N=170) | ASA 100 mg/day, clopidogrel 75 mg/day, GPIs | Timing: 1 yr  Composite  Total mortality  Nonfatal MI  Stroke  Rehospitalization  Individual  Major bleeding  Minor bleeding  Total mortality  Stent thrombosis | Good |
| Roy, 2009161 | Observational  Single site in U.S.  Funding: NR  Timeframe: 04/2003–01/2007  Population  N=1,331 UA  Total N: 2889  Mean Age: 63 to 65  Female: 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 yr  Individual  Stent thrombosis | Poor |
| Ruiz-Nodar, 2008162 | Observational  2 sites in Europe  Funding: NR  Timeframe: 01/2001–12/2006  Population  64% NSTEMI  20% STEMI  16% Stable CAD  Total N: 426  Mean Age: 71  Female: 30%  Race: NR | Warfarin  (N=242) | ASA  (N=184) | Clopidogrel, ASA  warfarin + ASA+ clopidogrel (N= 213),  coumarin +ASA (N=8), coumarin + clopidogrel (N=16), coumarin N=5 | Timing: 5 yr  Composite  (primary)  Total mortality  Nonfatal MI  Revascularization  (secondary)  Stroke  Major bleeding  MACE  Individual  Total mortality  Nonfatal MI  Revascularization  Major bleeding  Minor bleeding | Good |
| Ruiz-Nodar, 2012163 | Observational  NR sites in Europe  Funding: NR  Timeframe: 1/2001-3/2008  Population  63% NSTEMI  23% STEMI  Total N: 590  Mean age: 72  Female: 28.8%  Race: NR | Warfarin | Non-OAC | clopidogrel 94% of the total population  ASA 89.6% of total population  warfarin 56.3% of total population  warfarin +ASA+clop 44.6% | Timing: 1 yr  Composite  (secondary)  Total mortality  Nonfatal MI  target vessel failure  Individual  Total mortality  Major bleeding | Fair |
| Sarafoff, 2010164 | Observational  2 sites in Europe  Funding: NR  Timeframe: 07/2002–12/2006  Population  N= 781 UA  N=2208 Stable CAD  Total N: 3408  Mean Age: 66 to 69  Female: 24%  Race: NR | PPI  (N=698) | No PPI  (N=2,640) | Clopidogrel, ASA  Clopidogrel 75 mg twice daily together with ASA 100 mg twice daily | Timing: 30 days  Composite  (secondary)  Nonfatal MI  Stent thrombosis  Individual  Stent thrombosis  Total mortality  Nonfatal MI  Major bleeding | Good |
| Schmidt, 2012165 | Observational  NR sites in Europe  Funding: Private Foundation  Timeframe: 01/2002-06/2005  Population  30.7% UA  Total N: 13,001  Mean Age: NR  Female: 28%  Race: NR | PPI  (N=2742) | No PPI  (N=10,259) | Clopidogrel  75 mg maintenance dose | Timing: In-hospital  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  Stent Thrombosis  Target lesion revascularization  Individual  CV mortality  Nonfatal MI  Target lesion revascularization | Poor |
| Schulz, 2009166 | Observational  2 sites in Europe  Funding: "No industry involvement" but does not specify source of funds  Timeframe: 07/2002–12/2006  Population  N= 1197 UA  N=561 NSTEMI  N=627 STEMI  N=1188 ACS  N=4431 Stable CAD  Total N: 6,816  Mean Age: 67  Female: 24%  Race: NR | Clopidogrel + ASA  Loading dose: 600 mg clopidogrel + 500 mg ASA  Maintenance 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 yr  Individual  Stent thrombosis  Hazard reduction per 1 days treatment continuation  Risk of stent thrombosis within 4 yr | Fair |
| Sibbald, 2010167 | Observational  247 sites location NR  Funding: Industry  Timeframe: 04/1999–2007  Population  30% UA  34% NSTEMI  36% STEMI  Total N: 44,426  Median Age: 69 to 72  Female: 33%  Race: NR | Nonsmoker + no early clopidogrel  In-hospital  (N=15,110)  Nonsmoker + early clopidogrel  In-hospital  (N=17,167) | Smoker + no early clopidogrel  In-hospital  (N=4,791)  Smoker + early clopidogrel  In-hospital  (N=7,358) | ASA, unfractionated heparin, fibrinolytics, GPIs  ASA, enoxaparin, unfractionated heparin, fibrinolytics, GPIs | Timing: In-hospital  Composite  (primary)  Total mortality  Nonfatal MI | Good |
| Simon, 2011168  FAST-MI | Observational  223 sites in Europe  Funding: Private Foundation, Industry  Timeframe: 10/2005–11/2005  Population  NSTEMI: % unreported  STEMI: % unreported  UA: 0%  Total N: 2744  Mean Age: 64 to 74  Female: 29.8%  Race: NR | Clopidogrel at 48 hrs  No PPI  (N=900)  PPI  (N=1,453) | No clopidogrel  No PPI  (N=233)  PPI  (N=158) | Clopidogrel | Timing: In-hospital, 1 yr  Composite  Total mortality  Nonfatal MI  Stroke  Individual  Total mortality  Nonfatal MI  Stroke  Major bleeding | Good |
| So, 2009169 | Observational  Single site in Canada  Funding: NR  Timeframe: 12/2003–11/2004  Population  52% UA/NSTEMI\  25% STEMI  19% Stable CAD  Total N: 1,840  Mean Age: 61 to 64  Female: 27%  Race: NR | ASA 81 mg/d  Maintenance dose: 81mg/d  (N=910) | ASA 325mg/d  Maintenance 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 yr  Composite  (primary)  Total mortality  Nonfatal MI  (secondary)  Total mortality  Nonfatal MI  Revascularization  Individual  Total mortality  Revascularization | Fair |
| Steinhubl, 2002170  CREDO | RCT  99 sites in U.S., Canada  Funding: Industry  Timeframe: 06/1999–04/2001  Population  53% UA  14% NSTEMI  33% Stable CAD  Total N: 2,116  Mean Age: 62  Female: 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 yr  Composite  (primary)  Total mortality  Nonfatal MI  Stroke  Individual  Major bleeding | Good |
| Stenestrand, 2005171  RIKS-HIA | Observational  38 sites in Europe  Funding: Government, Private foundation  Timeframe: 1995–2002  Population  29% STEMI  Total N: 6275  Mean Age: 75 to 79  Female: 38%  Race: NR | ASA  (N=3,768) | OAC  (N=1,848) | Thienopyridine  ASA and/or thienopyridine | Timing: 30 days, 1 yr  Individual  Total mortality | Good |
| Stockl, 2010172 | Observational  NR sites in U.S.  Funding: NR  Timeframe: 01/2004–12/2006  Population: NR  Total N: 2,066  Mean Age: 69  Female: 44%  Race: NR | PPI  (N=1,033) | No PPI  (N=1,033) | Clopidogrel | Timing: 1 yr  Individual  Rehospitalization | Good |
| Tentzeris, 2010173 | Observational  Single site in Europe  Funding: Private foundation  Timeframe: 01/2003–12/2006  Population  45% ACS  Total N: 1,210  Mean Age: 64  Female: 31%  Race: NR | PPI  (N=691) | No PPI  (N=519) | Clopidogrel, ASA  ASA (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 yr  Composite  Total mortality  Rehospitalization  Stent thrombosis  Individual  Total mortality  CV mortality  Rehospitalization  Stent thrombosis | Good |
| Tsai, 2011174 | Observational  NR sites in Asia  Funding: NR  Timeframe: Jan 2001-Dec 2006  Population:  NR  Total N: 3,580  Mean Age: 71  Female: 38%  Race: NR | Clopidogrel + PPI  (N=1,052)  3rd treatment arm: ASA + PPI  (N=1,203) | Clopidogrel  (N=1,325) | NR | Timing: 1 yr  Composite  (primary)  Nonfatal MI  Stroke  Rehospitalization  Individual  GI events | Good |
| Valgimigli, 2012175  PRODIGY | RCT  3 sites in Europe  Funding: Private Foundation  Timeframe: 12/2006–12/2008  Population  N= 365 UA  N=450 NSTEMI  N=648 STEMI  N=507 Stable CAD  Total N: 2013  Mean Age: 68  Female: 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 yr  Composite  (primary)  Total mortality  Nonfatal MI  Stroke  (secondary)  Total mortality  Nonfatal MI  (secondary)  Total mortality  Stroke  Individual  Total mortality  CV mortality  Stroke  Stent thrombosis  Minor bleeding | Good |
| Valkhoff, 2011176 | Observational  Single site in Europe  Funding: Private foundation  Timeframe: 01/1999–12/2008  Population:  NR  Total N: 23,655  Mean Age: 65  Female: 33%  Race: NR | PPI  (N=NR) | No PPI  (N=NR) | Clopidogrel | Timing: 1 yr  Individual  Nonfatal MI | Poor |
| Van Boxel, 2010177 | Observational  Multiple sites in Europe  Funding: Industry  Timeframe: Jan 2006-Dec 2007  Population:  NSTEMI % unknown  STEMI % unknown  Total N: 18,139  Mean Age: 66 to 69  Female: 36%  Race: NR | Clopidogrel + PPI  (N=5,734) | Clopidogrel  (N=12,405) | NR | Timing: 30 days, 1 yr  Composite  (primary)  Total mortality  Nonfatal MI  Stroke  UA  Individual  Nonfatal MI  UA  Stroke  Total mortality  Peptic ulcer disease | Fair |
| Wu, 2010178 | Observational  NR sites in Asia  Funding: Government  Timeframe: 07/2002–06/2005  Population  N= 5862 ACS  Total N: 6,300  Mean Age: 66  Female: NR  Race: NR | PPI  (N=311) | No PPI  (N=5,551) | Clopidogrel | Timing: 3 mo  Composite  (primary)  Total mortality  Rehospitalization  Individual  Rehospitalization  Revascularization  Total mortality | Good |
| Yusuf, 2001154  CURE | RCT  482 sites in U.S., Canada, UK, Europe, S. America, C. America, Africa, Australia/NZ  Funding: Industry  Timeframe: 12/1998–09/2000  Population  N= 9414 UA  N=3148 NSTEMI  Total N: 12,562  Mean Age: 64  Female: 38%  Race: NR | Clopidogrel  Loading dose: 300 mg  Maintenance dose: 75 mg daily  (N=6,259) | Placebo  Loading dose: 300 mg  Maintenance dose: 75 mg daily  (N=6,303) | ASA, unfractionated heparin, GPIs, low molecular weight heparins  ASA (75 to 325mg) daily. Patients in each group were to receive open label thienopyridine following PCI | Timing: 9 mo  Composite  (primary)  CV mortality  Nonfatal MI  Stroke  (primary)  CV mortality  Nonfatal MI  Stroke  Refractory ischemia  Individual  CV mortality  Nonfatal MI  Stroke  Refractory ischemia  Heart failure  Severe ischemia  Revascularization  Major bleeding  Minor bleeding | Good |
| Zairis, 2010179 | Observational  Single site in Europe  Funding: NR  Timeframe: Apr 2003-Jan 2005  Population  37% STEMI  23% Stable angina  40% UA/NSTEMI  Total N: 588  Mean Age: 62  Female: 18%  Race: NR | Omeprazole  (N=340) | No PPI  (N=248) | ASA 100-325 mg  Clopidogrel 75 mg | Timing: 1 yr  Composite  (primary)  CV mortality  Rehospitalization  Individual  Rehospitalization  CV mortality  Stent thrombosis  Revascularization | Good |
| Zeymer, 2008180  ACOS Registry | Observational  155 sites in Europe  Funding: NR  Timeframe: 06/2000–12/2002  Population  100% NSTEMI  42% PCI  Total N: 4,290  Median Age: 67 to 72  Female: 27%  Race: NR | ASA + clopidogrel  (N=2119) | ASA  (N=2171) | NR | Timing: In-hospital, 1 yr  Composite  (primary)  Total mortality  Nonfatal MI  Nonfatal stroke  Individual  Total mortality  Nonfatal MI  Stroke | 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