**Appendix Table E17. Results from studies assessing the ability of LTA to predict major adverse cardiovascular events in patients with ischemic heart disease**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author,year****UID****Country****Study name** | **Treatment** | **Phenotypic Test Used [index test]** | **Clinical Outcome** | **Outcome Definition** | **Timing of measurement** | **Index test result: category (e.g., HPR+) – ONE ROW PER PHENOTYPE GROUP** | **Outcome status (e.g., bleeding or no bleeding)** | **No. with outcome status within phenotype group** | **Comparative metric (OR, RR, HR)** | **95% CI** | **P (between which groups?)****[statistical test]** | **Adjusted?****[YES/NO/NR]****If YES, for what factors?** | **Procedures for multiple comparisons [YES, NO, NR]** | **Comments (e.g., additional data in figures)** |
| Geisler 2010{Geisler, 2010 54 /id}20526607GermanyNR | Clopidogrel+aspirin | Lumi-aggregometer | MACE | MI, cardiovascular events, and cardiovascular death | 30 days after PCI | Top tertile of platelet aggregation (among the total 413 DM patients followed for 30 days)N=NR | MACE | NR | NR | NR | 0.02 (log-rank test) vs. DM patients in lowest tertile | NR | NR | K-M curve in Fig 6 |
| Frere, 2007{Frere, 2007 193 /id}17938809FranceNR | 600 mg loading dose of clopidogrel and maintaining 75mg daily  | ADP-induced platelet aggregation(ADP-Ag) | CV event | CV death, acute or subacute stent thrombosis, recurrent ACS and stroke | 30 days after PCI | ≥70%N=54  | CV event | 11/54 (20%)  | AUC: 0.74±0.08 | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | <70%N=127 | CV event | 3/127(2.5%) | OR (calculate)=10.6 | 2.8-39.7 | P value=0.000125(≥70% vs <70%)[Fisher’s exact test] |  |  |  |
| Breet 2010{Breet, 2010 86 /id}20179285NetherlandsPOPULAR | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily  | ADP LTA 5µmol/L | Death combined  | All-cause death, nonfatal MI, stent thrombosis and stroke | 1-year  | High OTPRN=445 | Death combined  | 52/445 (11.7) | OR=2.09 | 1.34-3.25 | <0.001 | No  | NR | Figure 1 KM curves |
|  |  |  |  |  |  | Normal OTPRN=604 |  | 36/604(6) |  |  |  |  |  |  |
|  | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily | ADP LTA 20 µmol/L | Death combined  | All-cause death, nonfatal MI, stent thrombosis and stroke | 1-year  | High OTPRN=392 | Death combined  | 47/392 (12) | OR=2.05 | 1.32-3.19 | <0.001 | No  | NR |  |
|  |  |  |  |  |  | Normal OTPRN=659 |  | 41/659(6.2) |  |  |  |  |  |  |
|  | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily  | ADP LTA 5µmol/L | Death combined  | All-cause death, nonfatal MI, stent thrombosis and stroke | 1-year  | High OTPR≥42.9%N=445 | Death combined  | 52/445 (11.7) | AUC: 0.63Sens: 0.602Spec: 0.591 | 0.58-0.680.498-0.6980.56-0.622 | NR | No  | NR |  |
|  | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily  | ADP LTA 20µmol/L | Death combined  | All-cause death, nonfatal MI, stent thrombosis and stroke | 1-year  | High OTPR≥64.5%N=392 | Death combined  | 47/392 (12) | AUC: 0.62Sens: 0.546Spec: 0.639 | 0.56-0.670.442-0.6450.608-0.668 | NR | No  | NR |  |
| Kim, 2010{Kim, 2010 241 /id}20449634KoreaNR | 300-600mg LD and 75 mg maintain dose clopidogrel  | 5umol/L ADP LTA | composite  | composite  | 6 months |  <50% | composite  | 2.2% | OR=2.69 | 1.37-5.29 | 0.003 | NR | NR |  |
|  |  |  |  |  |  | ≥50% |  | 5.6% |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Bliden,2007{Bliden, 2007 202 /id}17291930USANR | clopidogrel75 mg qd | ADP-induced platelet reactivity  | Total patients with ischemic events | Total patients with ischemic events | Day 0-30 | HPR n=22 | Total patients with ischemic events | 5/22 | OR (calculated)=27.0 | 8-91.4 | P value<0.0001(HPR vs NPR)[Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  | Day 0-30 | NPRN=78 | Total patients with ischemic events | 1/78 | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | Day 31-365 | HPR n=22 | Total patients with ischemic events | 11/22 |  |  |  |  |  |  |
|  |  |  |  |  | Day 31-365 | NPRN=78 | Total patients with ischemic events | 6/78 |  |  |  |  |  |  |
|  | clopidogrel75 mg qd | LTA | Ischemic events  | Ischemic events | NR  | HPR | Ischemic event | NR | OR=34.6 | 8.3-144.2 | <0.001 | Yes, age, presentation, diabetes, hypertension, current smoking, BMS(bare-metal stents) | NR |  |
| Gori,2008{Gori, 2008 151 /id}19132241Italy RECLOSE | Clopidogrel+aspirin | LTA-ADP | Stent thrombosis or cardiac death (composite) |  |  | RPR (n=90) |  | 8 | OR (calculated)=3.67 | NR | P value=0.006(RPR vs no RPR)[Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  |  | No RPR (n=656) |  | 17 | NR | NR |  | NR | NR |  |
|  |  | LTA-collagen |  |  |  | RPR (n=78) |  | 11 | OR (calculated)=7.67 | NR | P value=0.00001(RPR vs no RPR)[Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  |  | No RPR (n=668) |  | 14 | NR | NR |  | NR | NR |  |
|  |  | LTA-ADP | Stent thrombosis or cardiac death (composite) |  |  | RPR (n=90) |  |  | * 32% (15-54%) sensitivity
* 89% (86-91%) specificity
 |  | NS |  |  |  |
|  |  | LTA-collagen |  |  |  | RPR (n=78) |  |  | * 44% (25-63%) sensitivity
* 91% (88-93%) specificity
 |  | For specificity, “p<0.0001 vs RPR by collagen |  |  |  |
|  |  | LTA-ADP+LTA-collagen |  |  |  | RPR (n=31) |  | NA | * 28% (10-46%) sensitivity
* 97% (95-98%) specificity
 |  | For specificity, <0.01vs. LTA-ADP alone and vs. LTA-collagen | NR | NR |  |
|  |  | LTA-ADP among patients at high risk for AEs | Stent thrombosis or cardiac death (composite) |  |  | RPR (n=352) |  | NA | * 64% (45-83%) sensitivity
* 53% (50-57%) specificity
 |  | NS | NR | NR |  |
|  |  | LTA-collagen among patients at high risk for AEs |  |  |  | RPR (n=78) |  | NA | * 48% (28-68%) sensitivity
* 91% (89-93%) specificity
 |  |  | NR | NR |  |
|  |  | LTA-ADP+LTA-collagen among patients at high risk for AEs |  |  |  | RPR (n=61) |  |  | * 40% (21-59%) sensitivity
* 93% (91-95%) specificity
 |  | For sensitivity, p<0.01 vs. LTA-ADPFor specificity, p<0.0001 vs. LTA-ADP | NR | NR |  |
|  |  | LTA-ADP | Stent thrombosis or cardiac death (composite) |  |  | RPR |  |  | OR 3.67 | 1.53-8.76 | 0.003 Univariate analysis | NR | NR |  |
|  |  | LTA-collagen |  |  |  | RPR |  |  | OR 7.67 | 3.35-17.57 | 0.0001 Univariate analysis | NR | NR |  |
|  |  | LTA-ADP+LTA-collagen |  |  |  | RPR |  |  | OR 11.29 | 4.31-25.59 | 0.0001 Univariate analysis | NR | NR |  |
| Gurbel,2010{Gurbel, 2010 68 /id}20691842USAPREPARE POST-STENTING | Clopidogrel 300-600 mg LD + 75 mg MD &Aspirin 325 mg LD + 81-325 mg MD | LTA-ADP | MACE | Cardiac death, stent thrombosis, myocardial infarction, ischemicstroke, and unplanned revascularization | First event over f/u of 36 months | LTA-ADP >34% | MACE | NR | Sensitivity: 0.8Specificity: 0.59AUC: 0.75 | 0.68-0.8 | P<0.001 | NO | NR | Primary endpoint;14/59 (24%) of first events occurred after clopidogrel stopped (mean duration ofTx=of 6.4 ± 3 months) |
|  |  |  |  |  |  | LTA-ADP ≤34% |  | NR |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD &Aspirin 325 mg LD + 81-325 mg MD | LTA-ADP | MACE | Cardiac death, stent thrombosis, myocardial infarction, ischemicstroke, and unplanned revascularization | First event over f/u of 36 months | LTA-ADP >34% | MACE | NR | HR=4.8 | 2.4-9.6 | P<0.001 | NO | NR | Primary endpoint |
|  |  |  |  |  |  | LTA-ADP ≤34% |  | NR |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD &Aspirin 325 mg LD + 81-325 mg MD | LTA-ADP | MACE | Cardiac death, stent thrombosis, myocardial infarction, ischemicstroke, and unplanned revascularization1 | First event over f/u of 36 months | LTA-ADP >34% | MACE | NR | HR=5.6 | 2.7-11.6 | P<0.001 | YES;History of prior PTCA and calcium-channel blockers | NR | Primary endpoint |
|  |  |  |  |  |  | LTA-ADP ≤34% |  | NR |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD &Aspirin 325 mg LD + 81-325 mg MD | LTA-ADP | MACE | Cardiac death, stent thrombosis, myocardial infarction, ischemicstroke, and unplanned revascularization1 | First event over f/u of 36 months | Quartile 1 <65 mm  | MACE | 6 (11%) | NR | NR | NR | NR | NR | Primary endpoint |
|  |  |  |  |  |  | Quartile 2 65-69 mm |  | 8 (15%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 3 >69-72 mm |  | 16 (30%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 4 >72 mm |  | 29 (52%) |  |  |  |  |  |  |
| Matetzky,2004{Matetzky, 2004 188 /id}15184279Israel No | Clopidogrel | Aggregometer (not cone and platelet device) | Recurrent major adverse cardiovascular event | NR | 6 months after PCI | Q1 | Yes event | 6 (40%) | NR | NR | 0.007 for trend of Q1 through Q2, Q3 and Q4  | NR | NR | NO |
|  |  |  |  |  |  | Q2 |  | 1 (6.7%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Q3 |  | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Q4 |  | 0 |  |  |  |  |  |  |
| Angiolollo, 2007{Angiolillo, 2007 194 /id}17936152SpainNR | clopidogrel (75 mg/day) | LTA-ADP | MACE | Major adverse cardiovascular events  | 2 years | HPR cutoff 62%  | MACE | 37.7% | OR=3.96 | 1.8-8.7 | <0.001 comparing no-HPR | NR | NR |  |
|  |  |  |  |  |  | No HPR | MACE | 13.3% |  |  |  |  |  |  |
|  |  |  |  |  |  | HPR cutoff 62%  | MACE | 37.7% | OR=3.35 | 1.68-6.66 | 0.0013 comparing no-HPR | Yes, renal failure, New York Heart Assocaition functional class III to IV | NR |  |
|  |  |  |  |  |  | No HPR | MACE | 13.3% |  |  |  |  |  |  |
| Aradi 2008{Aradi, 2008 236 /id}18388039HungaryNR | Clopidogrel + aspirin | Platelet aggregometry | Cumulative event-free survival(events were cardiovascular death, myocardial infarction, revascularization, in-stent restenosis, stent thrombosis, or de novo lesion) | All deaths regarded as cardiovascular unless clear evidence of any other non-cardiovascular cause. MI defined as presence of at least 2 of the 3 criteria: typical chest pain, new ECG changes compatible with MI (Q-wave duration >0.04 sec or >1/4 of the corresponding R-wave’s amplitude, ST segment elevation in >2 relevant leads over 0.1 mV), elevation of CK and CK-MB >2xULN in at least 2 different samples. Revascularizations included repeated PCI and CABG.  | 10 mo after stenting | Below 50th percentile of maximal ADP 5 mcmol aggregation | ~60% eyeballed estimate | NR | NR | NR | <0.01 vs. next row (Kaplan-Meier test) | NR | NR | Fig 2A has survival curves |
|  |  |  |  |  |  | Above 50th percentile of ADP 5 mcmol aggregation | ~93% eyeball estimate |  |  |  |  |  |  |  |
| Breet, 2011{Breet, 2011 15 /id}21478385The NetherlandsPOPular | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | LTA5 | Death, MI, ST, stroke | Death, MI, ST, stroke | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR | Death, MI, ST, stroke | 43/385 | NR | NR | 0.009 (HCPR vs NPR)  | NR | NR | Kalpak-Meier curves (figure 1) |
|  | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily  | LTA20 | Death, MI, ST, stroke | Death, MI, ST, stroke | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR | Death, MI, ST, stroke | 37/355 | NR | NR | 0.006 (HCPR vs NPR) | NR | NR |  |
|  | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | LTA5 | Death, MI, ST, stroke | Death, MI, ST, stroke | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR | Death, MI, ST, stroke | NR | OR=2.63  | 1.17-5.92 | 0.02(HCPR vs NPR)[Logistic regression] | Yes, age, impaired ejection fraction, LTA5: HAPR, LTA20 HAPR, hypertension, LTA20 HCPR, LTA5 DAPR, LTA20 DAPR, graft-stenting, bifurcation lesion, verifynow DAPR | NR |  |
|  | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | LTA20 | Death, MI, ST, stroke | Death, MI, ST, stroke | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR | Death, MI, ST, stroke | NR | OR=3.31 | 1.47-7.5 | 0.004(HCPR vs NPR)[Logistic regression] | Yes, age, impaired ejection fraction, LTA5: HAPR, LTA20 HAPR, hypertension, LTA5 HCPR, LTA5 DAPR, LTA20 DAPR, graft-stenting, bifurcation lesion, verifynow DAPR | NR |  |
| Breet 2010{Breet, 2010 50 /id}20695984NetherlandsSubstudy of a larger cohort (Breet 2010 PMID: 20179285) | Clopidogrel 300-900 LD + 75 mg MD | LTA with 20 µmol/L | MACE | All-cause death, nonfatal MI, definite stent thrombosis and ischemic stroke | 1-year  | High on-treatment platelet reactivity with native platelet rich plasma | MACE | 30 | OR=2.45 | 1.45-4.15 | P=0.001 | No  | NR |  |
|  |  |  |  |  |  | Normal on-treatment platelet reactivity with native platelet rich plasma |  | 33 |  |  |  |  |  |  |
|  | Clopidogrel 300-900 LD + 75 mg MD | LTA with 20 µmol/L | MACE | All-cause death, nonfatal MI, definite stent thrombosis and ischemic stroke | 1-year  | High on-treatment platelet reactivity with adjusted platelet rich plasma | MACE | 30 | OR=1.78 | 1.05-2.99 | P=0.04 | No  | NR |  |
|  |  |  |  |  |  | Normal on-treatment platelet reactivity with adjusted platelet rich plasma |  | 33 |  |  |  |  |  |  |
|  | Clopidogrel 300-900 LD + 75 mg MD | LTA with 20 µmol/L | MACE | All-cause death, nonfatal MI, definite stent thrombosis and ischemic stroke | 1-year  | High on-treatment platelet reactivity with native platelet rich plasma | MACE | 30 | AUC=0.59 | 0.52-0.66 | NR | No  | NR |  |
|  | Clopidogrel 300-900 LD + 75 mg MD | LTA with 20 µmol/L | MACE | All-cause death, nonfatal MI, definite stent thrombosis and ischemic stroke | 1-year  | High on-treatment platelet reactivity with adjusted platelet rich plasma | MACE | 30 | AUC=0.59 | 0.52-0.66 | NR | No  | NR |  |
| Buonamici, 2007{Buonamici, 2007 200 /id}17572245ItalyNR | Clopidogre l LD 600 mg maintenance dose of 75 mg daily  | LTA ADP | Composite of cardiac death and stent thrombosis  | Composite of cardiac death and stent thrombosis  | 6 months  | Responders | Composite of cardiac death and stent thrombosis  | 19/699(2.7) | NR | NR | <0.001 comparing with the following group  | NR | NR  |  |
|  |  |  |  |  |  | Non-responders  |  | 11/105(11) |  |  |  |  |  |  |
| Campo, 2007{Campo, 2007 197 /id}17868803ItalyNR | Clopidogrel 300-mg loading dose, followed by 75 mg/day | LTA ADP | MACE | MACE | 6 months  | Responder to both | MACE | 2(2.2) | OR (calculated)=2.43 | 0.7-8.5 | P value=0.169(clopidogrel and dual nonresponders vsother groups)[Fisher’s exact test] | NO | NR |  |
|  |  |  |  |  |  | Clopidogrel –Ticlopidine+ |  | 3(12) |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel +Ticlopidine -  |  | 5(22) |  |  |  |  |  |  |
|  |  |  |  |  |  | Nonresponder to both |  | 2(40) |  |  |  |  |  |  |
| Cuisset 2006{Cuisset, 2006 212 /id}16371119FranceNR | Clopidogrel+aspirin | PAP4 aggregometer | Cardiovascular event | CV death, acute or subacute stent t hrombosis, ischemic stroke and recurrent ACS | 1 month | Q1-Q3 (responder) | Yes event | 3 (4%) | NR | NR | NR | NO | NR | NO |
|  |  |  |  |  |  |  | No event | 80 (96%) | NR | NR | NR | NO |  |  |
|  |  |  |  |  |  | Q4 (nonresponder) | Yes event | 9 (39%) | OR vs Q1-3: 22.4 | 4.6-109 | <0.05 (l ogistic regression) vs. Q1-3 yes event | NO |  |  |
|  |  |  |  |  |  |  |  |  | OR vs Q1-3:19.6  | 4.24-90.3 | <0.001 (l ogistic regression) vs. Q1-3 yes event | YES age, sex |  |  |
|  |  |  |  |  |  |  |  |  | OR vs Q1-3:35 | 4.81-248 | <0.001 (l ogistic regression) vs. Q1-3 yes event | YES age, sex, (hypertension, diabetes, dyslipidemia, smoking, ejection fraction), heart rate, systolic blood pressure and treatments. |  |  |
|  |  |  |  |  |  |  |  |  | OR vs Q1-3:41.6 | 4.74-364 | 0.003 (l ogistic regression) vs. Q1-3 yes event | YES age, sex, (hypertension, diabetes, dyslipidemia, smoking, ejection fraction), heart rate, systolic blood pressure and treatments + P-selectin and CRP |  |  |
|  |  |  |  |  |  |  | No event | 14 (61%) |  |  |  |  |  |  |
| Cuisset 2006{Cuisset, 2006 237 /id}17010792FranceNR | Clopidogrel 300 mg LD | LTA | CV events | CV death, acute or subacute stentthrombosis, recurrent ACS, and stroke. | 1 month | high post treatment platelet reactivity  | CV events | 12 | OR=9.93 | 3.19-30.9 | NR[logistic regression] | YES;Age, gender | NR |  |
|  |  |  |  |  |  | normal post treatment platelet reactivity |  | 6 |  |  |  |  |  |  |
|  | Clopidogrel 600 mg LD | LTA | CV events | CV death, acute or subacute stentthrombosis, recurrent ACS, and stroke. | 1 month | high post treatment platelet reactivity  | CV events | 6 | OR=43.16 | 4.89-381.1 | NR[logistic regression] | YES;Age, gender | NR |  |
|  |  |  |  |  |  | normal post treatment platelet reactivity |  | 1 |  |  |  |  |  |  |
| Geisler 2008{Geisler, 2008 184 /id}17949474GermanyNR | Clopidogrel  | Turbidoaggregometry | Major adverse events (MI, ischemic stroke, death, or cardiovascular death |  | 30 days | RPA tertile 1 (lowest) | Yes event | 5 (1.5%) | OR (calculated)=2.37 | 1.1-5 | P value=0.026(highest tertile vs tertile 1&2)[Fisher’s exact test] | NO (not for these data) | NR | These data are for 950 patients (87% of the 1092) with 30-day followup data |
|  |  |  |  |  |  | RPA tertile 2 |  | 8 (2.5%) |  |  |  |  |  |  |
|  |  |  |  |  |  | RPA tertile 3 (highest) |  | 15 (4.8%) |  |  |  |  |  |  |
| Geisler, 2006{Geisler, 2006 210 /id}17005534GermanyNR | Clopidogrel LD dose of 600 mg followed 75 mg daily | ADP LTA | Composite CV endpoints  | Composite CV endpoints  | 3-month | Adequate response  | Composite CV endpoints  | 19/341 (5.6) | NR | NR | 0.01 | NR | NR |  |
|  |  |  |  |  |  | Low response  |  | 5/22 (22.7) |  |  |  |  |  |  |
|  | Clopidogrel LD dose of 600 mg followed 75 mg daily | ADP LTA | Cumulative events  | Cumulative events  | 3-month | Adequate response  | Cumulative events  | 23/341 (6.7) | NR | NR | 0.005 | NR | NR |  |
|  |  |  |  |  |  | Low response  |  | 6/22 (27.3) |  |  |  |  |  |  |
|  | Clopidogrel LD dose of 600 mg followed 75 mg daily | ADP LTA | Composite cardiovascular endpoints | Composite cardiovascular endpoints | 3 months | Low response  | Composite cardiovascular endpoints | N=22 | HR=3.71 | 1.08-12.69 | 0.04 | Yes, factors influencing cardiovascular outcome | NR |  |
| Geisler 2010{Geisler, 2010 101 /id}19812059GermanyNR | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | MACE | MI, ischemic stroke, cardiovascular death | 3 months | Low responder (Terrtile 3) | MACE | 30 (4.2%) | OR=2.21 | 1.31-3.73 | p=0.002(low responder vs responder)[chi square] | NO | NR | Secondary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | 30 (9.1%) |  |  |  |  |  |  |
| Giusti, 2009{Giusti, 2009 134 /id}19268736ItalyRECLOSE study(Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | Aspirin (loading dose = 325 mg; maintenance dose = 325 mg per day) and clopidogrel (loading dose = 600 mg; 75 mg maintenance). | LTA- ADP | MACE | Composite of cardiac mortality and stent thrombosis (definite or probable) | Maximum FU of 6 mo | Residual platelet reactivity (RPR) (ADP-induced platelet aggregation ≥70%) | Cardiac death or stent thrombosis | 10 (9.1%) | NR | NR | 0.001 across groups (chi square test) | NO | NO | Secondary outcome |
|  |  |  |  |  |  | No residual platelet reactivity (RPR)  |  | 19 (2.1%)­ |  |  |  |  |  |  |
|  | Aspirin (loading dose = 325 mg; maintenance dose = 325 mg per day) and clopidogrel (loading dose = 600 mg; 75 mg maintenance). | Combination of genotypic and phenotypic tests: CYP2C19\*2 + ADP residual platelet reactivity (see also KQ1b extraction form) | MACE | Composite of cardiac mortality and stent thrombosis (definite or probable) | Maximum FU of 6 mo | \*2/\*2 + RPRN = 40 | Cardiac death or stent thrombosis | 7 (17.5%) | NROR=11.45 | NR(1.84, 71.27) | <0.0001 (chi square test)0.009 (logistic regression) | NOAdjusted (“for traditional cardiovascular risk factors and clinical and procedural risk factors for stent thrombosis”) | NO | Secondary outcome |
|  |  |  |  |  |  | \*1/\*1 or low RPRN = 732 |  | 22 (3%) |  |  |  |  |  |  |
|  | Aspirin (loading dose = 325 mg; maintenance dose = 325 mg per day) and clopidogrel (loading dose = 600 mg; 75 mg maintenance). | LTA-ADP | MACE | Composite of cardiac mortality and stent thrombosis (definite or probable) | Maximum FU of 6 mo | Residual platelet reactivity (RPR) (ADP-induced platelet aggregation ≥70%) | Cardiac death or stent thrombosis | 10 (9.1%) | OR=3.38OR=2.9 | (1.53, 7.49)(1.08, 12.98) | 0.003 (chi square test)0.019 (logistic regression) | NO (univariate)YES (ADP-RPR, traditional cardiovascular risk factors, clinical and procedural risk factors for ST) | NO | Secondary outcome |
|  |  |  |  |  |  | No residual platelet reactivity (RPR)  |  | 19 (2.1%) |  |  |  |  |  |  |
| Gori 2008 {Gori, 2008 164 /id}18718420ItalyRECLOSE study(Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | MACE | Cardiac death & stent thrombosis | 6 months | Clopidogrel nonresponder  | Cardiac death & stent thrombosis | NR | HR=2.23 | 0.85 to5.82 | P=0.101 | YES;age (years), male gender, family history of CAD, smoker, HTN, hypercholesterolemia, diabetes mellitus, history of myocardial infarction, history of coronary surgery, acute coronary syndrome, acute STEMI, left ventricular ejection fraction (%), multivessel disease, bifurcation lesion, thrombus-containing lesion, chronic total occlusion, and stent length (mm). | NR | Secondary endpoint |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | MACE | Cardiac death & stent thrombosis | 6 months | Clopidogrel & Aspirin nonresponder  | Cardiac death & stent thrombosis | NR | HR=2.94 | 1.17 to7.41 | P=0.022 | YES;age (years), male gender, family history of CAD, smoker, HTN, hypercholesterolemia, diabetes mellitus, history of myocardial infarction, history of coronary surgery, acute coronary syndrome, acute STEMI, left ventricular ejection fraction (%), multivessel disease, bifurcation lesion, thrombus-containing lesion, chronic total occlusion, and stent length (mm). | NR | Secondary endpoint |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | MACE | Cardiac death & stent thrombosis | 6 months | Clopidogrel responder and Aspirin responder | Cardiac death & stent thrombosis | 15 (2.6) | NR | NR | P<0.0001; (dual clopidogrel and aspirin nonresponders versus aspirin nonresponders)P<0.05; (dual clopidogrel and aspirin nonresponders versus aspirin nonresponders) | NO | NR | Secondary endpoint |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin nonresponder |  | 6 (13.3) |  |  | p <0.05 (dual clopidogrel and aspirin nonresponders versus aspirin nonresponders)p <0.0001 (dual clopidogrel and aspirin nonresponders versus aspirin nonresponders) |  |  |  |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin responder  |  | 2 (4.4) |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel responder and aspirin nonresponder |  | 2 (2.3) |  |  |  |  |  |  |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | MACE | Cardiac death & stent thrombosis**Error! Bookmark not defined.** | 6 months | Clopidogrel responder and Aspirin responder | Cardiac death & stent thrombosis | NR | NR | NR | P<0.0001; (dual nonresponders vs. dualresponder)P=0.011 (dual nonresponders vs. aspirinnonresponders)P=0.127(dual nonresponders vs. clopidogrelnonresponders) | NO | NR | Secondary endpoint |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Gurbel, 2008{Gurbel, 2008 157 /id}19012177USANone | Clopidogrel+aspirin | 5 mcM ADP aggregation | Any first ischemic event | Death, MI, stent thrombosis, revascularization (target or nontarget vessel), stroke, rehospitalization for ischemia without revascularization  | 1 mo | >46% platelet aggregation (HPR) | YES event | 4 (5%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 47 (53%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 1 mo | <=46% |  | 5 (2%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 25 (12%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  |  |  |  | AUC 0.77;Also sensitivity 63%, specificity 82% | NR | 0.0001 |  |  | 95% CIs are in Fig 3 |
|  | Clopidogrel+aspirin | 5 mcM ADP aggregation | Any first ischemic event |  | 0-24 mo | >46% platelet aggregation (HPR) |  | 51 (58%) | HR vs. next row, 3.9 | 1.9-8.4 | 0.001 vs. next row (Fisher’s exact and also multivariate Cox regression for HR) | NR | NR | NR |
|  |  |  |  |  |  | <=46% |  | 30 (14%) | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 20 mcM ADP aggregation | Any first ischemic event | Death, MI, stent thrombosis, revascularization (target or nontarget vessel), stroke, rehospitalization for ischemia without revascularization  | 1 mo | >59% platelet aggregation (HPR) | YES event | 4 (4%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 50 (50%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 1 mo | <=59% |  | 5 (3%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 22 (11%) | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  |  |  |  | AUC 0.78;Also sensitivity 68%, specificity 78% | NR | 0.0001 |  |  | 95% CIs are in Fig 4 |
|  | Clopidogrel+aspirin | 20 mcM ADP aggregation | Any first ischemic event |  |  | >59% platelet aggregation (HPR) |  | 54 (54%) | HR vs. next row, 3.8 | 1.8-7.9 | 0.001 vs. next row (Fisher’s exact and also multivariate Cox regression for HR) | NR | NR | NR |
| Gurbel, 2004{Gurbel, 2004 220 /id}15154601USANone | Clopidogrel+aspirin | Aggregometry | Stent thrombosis, target vessel revascularization, cerebrovascular ischedmic event, or death | NR | Within 30 days after PCI | Heightened reactivity | Yes event | 0 | NR | NR | NR | NR | NR | NO |
|  |  |  |  |  |  | No heightened reactivity |  | 0 |  |  |  |  |  |  |
| Hochholzer, 2006{Hochholzer, 2006 208 /id}17084243GermanyEXCELSIOR | Clopidogrel 75 mg/day | ADP LTA | Any MACE | Any MACE | 30-day | 1st quartile <4% | Any MACE | 209 | Mean 1(0.5) | NR | 0.03 | NR | NR |  |
|  |  |  |  |  |  | 2nd quartile 4-14%  |  | 198 | 1(0.5) |  |  |  |  |  |
|  |  |  |  |  |  | 3rd quartile15-32%  |  | 196 | 6 (3.1) |  |  |  |  |  |
|  |  |  |  |  |  | 4th quartile>32%  |  | 199 | 7(3.5) |  |  |  |  |  |
|  | Clopidogrel 75 mg/day | ADP LTA | Any MACE or major bleeding | Any MACE or major bleeding | 30-day | 1st quartile <4% | Any MACE or major bleeding | 209 | Mean 4(1.9) | NR | 0.44 | NR | NR |  |
|  |  |  |  |  |  | 2nd quartile 4-14%  |   | 198 | 3(1.5) |  |  |  |  |  |
|  |  |  |  |  |  | 3rd quartile15-32%  |  | 196 | 7(3.6) |  |  |  |  |  |
|  |  |  |  |  |  | 4th quartile>32%  |  | 199 | 7(3.5) |  |  |  |  |  |
|  | Clopidogrel 75 mg/day | Platelet aggregation(PA) | MACE | Major adverse cardiac event  | 30 days | 10% increase in ADP-induced PA | MACE | NR | OR=1.32 | 1.04-1.61 | 0.026 | Yes. Demographic, clinical and angiographic variables, time from clopidogrel loading and baseline platelet aggregation  | NR |  |
|  |  |  |  |  |  |  |  |  | OR=1.31 | 1.03-1.67 | 0.026 | No  |  |  |
| Htun, 2011{Htun, 2011 20 /id}21273381GermanyNR | clopidogrel LD 600 mg then 75 mg/d and aspirin 100mg/d | LTA ADP | combined major event within follow-up | myocardial infarction, ischemic stroke, and death | 1 year | low-responder group | combined major event within follow-up | 326/1567 | HR=2.08 | 1.42-3.03 | <0.001 comparing with responder  | no | NR |  |
|  | clopidogrel LD 600 mg then 75 mg/d and aspirin 100mg/d | LTA ADP | combined major event within follow-up | myocardial infarction, ischemic stroke, and death | 1 year | low-responder group | combined major event within follow-up | 326/1567 | HR=1.64 | 1.06-2.54 | 0.026 comparing with responder  | yes, diabetes mellitus, acute coronary syndromes, impaired left ventricular, gender arterial hypertension, tobacco use, age, cardiovascularcomedication, antiplatelet pretreatment, clopidogrel low response, and age. | NR |  |
| L’Allier 2008{L'Allier, 2008 178 /id}18342223CanadaPREPAIR study | clopidogrel LD 600 mg then 75 mg/d and aspirin 100mg/d | LTA ADP | combined major event within follow-up | myocardial infarction, ischemic stroke, and death | 1 year | low-responder group1  | combined major event within follow-up | 30/165(18.2) | NR | NR | 0.038 comparing with the lower row | NR | NR |  |
|  |  |  |  |  |  | responder group 1 |  | 46/396 (11.6) |  |  |  |  |  |  |
|  |  |  |  |  |  | low-responder group 2 |  | 11/161(6.8) |  |  | 0.59 comparing with the lower row |  |  |  |
|  |  |  |  |  |  | responder group 2 |  | 35/613(5.7) |  |  |  |  |  |  |
|  | Clopigogrel—Group A, B, and C (differing clopidogrel regimens) | Aggregometry | Major bleeding, death, rehospitalization for MI, or repeat target-vessel revascularization | Major bleeding deﬁned as intracranial or clinically relevant bleeding with decrease in hemoglobin of >5 g/dl | within 1 mo after discharge | All nonresponder groups as listed above | Yes event | 0 in each group | NR | NR | NR | NO | NO | Each outcome here reporter independently in paper |
| Liu 2011{Liu, 2011 12 /id}21613806ChinaNone | Clopidogrel+aspirin | Aggregometry | Any CV event | NR | 1 mo after stenting | Nonrespoders | 34 | 6 | NR | NR | NR | NR | NR | For all clinical data, n=106 patients because 3 more were lost to followup |
|  |  |  |  |  |  | Low responders | 28 | 2 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responders | 44 | 0 |  |  | 0.014 across this and previous 2 rows (chi-square test) |  |  |  |
|  | Clopidogrel+aspirin | Aggregometry | Any CV event |  | 3 mo after stenting | Nonrespoders | 34 | 11 |  |  |  |  |  |  |
|  |  |  |  |  |  | Low responders | 28 | 2 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responders | 44 | 0 |  |  | <0.0001 across this and previous 2 rows (chi-square test) |  |  |  |
| Muller, 2010{Muller, 2010 51 /id}20728084GermanyNR | Clopidogrel 600 mg LD + 75 mg MD & Aspirin 100 mg/d MD | LTA | MACE | composite of myocardial infarction and death | Mean follow up of 344 days | Stratum I: RPA & CRP <median | MACE | NR | NR | NR | P<0.001(Stratum IV vs I)P<0.001(Stratum IV vs II)P=0.06(Stratum IV vs III)P=0.01(Stratum III vs I)P>0.05(Stratum III vsI I)P>0.05(Stratum II vs I)[Log Rank ]test | YES;age,gender, left ventricular function, acute coronary syndromes, hyperlipidemiaand relevant comedication | NR | Primary |
|  |  |  |  |  |  | Stratum II:RPA >median & CRP ≤median |  | NR |  |  |  |  |  |  |
|  |  |  |  |  |  | Stratum III:RPA ≤ median & CRP >median |  | NR |  |  |  |  |  |  |
|  |  |  |  |  |  | Stratum IV:RPA & CRP >median |  | NR |  |  |  |  |  |  |
|  | Clopidogrel 600 mg LD + 75 mg MD & Aspirin 100 mg/d MD | LTA | MACE | composite of myocardial infarction and death | Mean follow up of 344 days | By Quartiles (not defined) | MACE | NR | NR | NR | NR | NO | NR | “Most events occurred in patients with a platelet aggregation in the upper quartile of the collective” |
| Trenk, 2008{Trenk, 2008 171 /id}18482659GermanyEXCELSIOR (Impact of Extent of Clopidogrel- Induced Platelet Inhibition During Elective Stent Implantationon Clinical Event Rate) | 600 mg clopidogrel LD + 75 mg/day MD (for 30 d w/ bare-metal stents or 6 mth w/ atleast 1 drug-eluting stent | LTA | Composite of death and MI | MI: new rise introponin T ≥0.03 mg/l associated with typical symptomsand/or typical electrocardiogram changes and/or typicalangiographic findingDeath: as reported in phone interview | 1 year | high on-treatment plateletreactivity (RPA>14%)  | MI or death | 13/217 (6%) | HR= 3 | 1.4-6.8 | P=0.004 (between high and not high residual platelet reactivity) | YES;Age, HTN, DM, BMI, platelet count, verapamil, insulin and antidiabetic medication use, previous angioplasty and CABG, LV function, angina class, PCI, stent implantation, LAD affected, stenosis length ad diameter of stenosis  | NR | Primary outcome |
|  |  |  |  |  |  | no high on-treatment plateletreactivity (RPA≤ 14%) |  | 11/548 (2%) |  |  |  |  |  |  |
| Wang, 2010{Wang, 2010 37 /id}21171668ChinaNone | Clopidogrel+aspirin | LTA | composite of cardiovascular death, MI and revascularization | death of acute MI, coronary artery disease, or heart failure; any typical increase or decrease of cardiac biomarker along with clinical symptoms consis ent with cardia c ischemia, following the American College of Cardiology definition; or bypass surgery and PCI | Within 1 yr after discharge | Clopidogrel resistance | YES event | 7 (21.88%) | NR | NR | 0.006 vs. next row (Student’s t);P=0.008 from multivariate regression (for indpendent prediction) | YES for multivariate regression P value only (diabetes, BMI, and smoking status) | NR | NONE |
|  |  |  |  |  |  | nonresistance |  | 6 (4.92%) |  |  |  |  |  |  |
| Wang, 2009{Wang, 2009 130 /id}19041120ChinaNR | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | Composite thrombotic events  | Cardiovascularf death, confatal-MI stent thrombosis or CVA | 12-months | Clopidogrel resistancce  | Cardiovascularf death, confatal-MI stent thrombosis or CVA | NR | HR=2.44 | 1.09-5.45 | 0.031 | Yes, diabetes , LV dysfunction (EF<30%) | NR |  |
|  | LD 300 mg clopidogrel and maintaining 75 mg daily  | ADP-LTA | Composite end points | Cardiovascularf death, confatal-MI stent thrombosis or CVA | One year  | Clopidogrel resistance  | Composite end points | 11/65 (16.9) | NR | NR | 0.01comparing with the following group | NO | NO  | 2 Kaplan-Meier curves for 12-month event-freee survival from composite thrombotic events |
|  |  |  |  |  |  | Normal response  |  | 20/321(6.2) |  |  |  |  |  |  |
|  |  |  |  |  |  | Total  |  | 31/386(8.0) |  |  |  |  |  |  |
| Yong, 2009{Yong, 2009 146 /id}19081397AustraliaPlatelet Responsiveness to Aspirin and Clopidogrel andTroponin Increment after Coronary intervention in Acutecoronary Lesions (PRACTICAL) Trial | 300-600 mg LD of clopidogrel | LTA using 4 , 10, 20μmol/L | MACE | death, nonfatal MI, nonfatal stroke, hospitalization for recurrent ischemia | 6 months | Quartile 1 | Post-PCI myonecrosis | NR | NR | NR | NR | NR | NR | Data presented in Fig 2B; no pvalues are reporter for all concentrations of ADP |
|  |  |  |  |  |  | Quartile 2 | NR |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 3 | NR |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 4 | NR |  |  |  |  |  |  |  |
| Gurbel, 2005{Gurbel, 2005 215 /id}16286165USAPREPARE POST-STENTING | Clopidogrel (300- 600 mg LD+75 mg daily MD) + aspirin (81- to 325-mg/d x 7 days LD + 325 md/f MD) | LTA | Ischemic events | Cardiovascular death, MI, unstable angina and stroke requiring rehospitalization | 6 months | High LTA - Quartile 4 (>67%) | Ischemic events | NR | OR=2.7 | 0.565-12.964 | P=0.2129(Mulitple logistic regression) | NO | YES;Low TEG-R (reaction time<3.9 mins), High TEG-MA (Max amplitude >72 mm) and combination of High TEG-MA and low R | Tab 4; it’s not clear if all predictor were in the same model |
|  | Clopidogrel (300- 600 mg LD+75 mg daily MD) + aspirin (81- to 325-mg/d x 7 days LD + 325 md/f MD) | LTA | Ischemic events | Cardiovascular death, MI, unstable angina and stroke requiring rehospitalization | 6 months | High LTA - Quartile 4 (>67%) | Ischemic events | NR | Sens=0.37Spec=0.79 | NR | NR | NO | No |  |
|  | Clopidogrel (300- 600 mg LD+75 mg daily MD) + aspirin (81- to 325-mg/d x 7 days LD + 325 md/f MD) | LTA | Ischemic events | Cardiovascular death, MI, unstable angina and stroke requiring rehospitalization | 6 months | Quartile 1 (<50%) | Ischemic events | 10% | NR | NR | P=0.02 (Q1 vs Q4)P=0.35 (Q2 vs Q4)P=0.37 (Q3 vs Q4)Logistic regression with appropriate contrasts | NO | NR | Fig 4 |
|  |  |  |  |  |  | Quartile 2 (50-61%) |  | 24% |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 3 (62-67%) |  | 22% |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 4 (>67%) |  | 32% |  |  |  |  |  |  |
| Angiolillo, 2011 {Angiolillo, 2011 18175 /id}ItalyNR | aspirin 100mg/day indefinitely and clopidogrel 75mg/day for 12 months | LTA-ADP | MACE | composite of cardiovascular death, ACS leading to hospital stay, nonfatal stroke | 24 months | HPR N=47 | MACE | 13 (28%) | HR=2.9 | 1.38-6.11 | 0.005(HRP vs no HPR)[Cox regression] | No | NR |  |
|  |  |  |  |  |  | No HPR N=140 |  | 15 (10.9%) |  |  |  |  |  |  |
|  |  |  |  |  |  | HPR N=47 | MACE | 13 (28%) | HR=3.1 | 1.47-6.52 | 0.003(HRP vs no HPR)[Cox regression] | yes, variable from table 1 | NR |  |
|  |  |  |  |  |  | No HPR N=140 |  | 15 (10.9%) |  |  |  |  |  |  |
| Saad, 2012{Saad, 2012 18187 /id}22146578EgyptNR | clopidogrel LD: 600 mg; MD: 75 mg/d; aspirin 162 mg/d | LTA-ADP | MACE | CV death, recurrent acute coronary syndrome (ACS), and acute,subacute, and late stent thromboses | 6 months | ≥12.5%N=NR | MACE | NR | AUC=0.793 | 0.674-0.913 | P<0.001 | No | NR |  |
|  |  |  |  |  |  | <12.5%N=NR |  | NR |  |  |  |  |  |  |
| Aradi {Aradi, 2012 18248 /id}21902692HungaryNR | LD clopidogrel 600mg and aspirin 300mgMD clopidogrel 75 mg/day 4 weeks | LTA ADP | CV death and MI | CV death and MI | 12 months | NPR | CV death and MI | 9/122=9.5% | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | HPR+150 mg clopidogrel  | CV death and MI | 1/36=3.1% | OR=14.2(calculated) | 1.54-131.61 | 0.09 comparing with the low rowlog-rank test  |  |  |  |
|  |  |  |  |  |  | HPR +75 mg clopidogrel  | CV death and MI  | 5/38=16.4% |  |  |  |  |  |  |
| Aradi {Aradi, 2012 18248 /id}21902692HungaryNR | LD clopidogrel 600mg and aspirin 300mgMD clopidogrel 75 mg/day 4 weeks | LTA ADP | CV death , MI or TVR | CV death , MI or TVR | 12 months | NPR | CV death , MI or TVR | 9/122=9.5% | OR=3.35 (calculated)  | 1.19-9.42 | NR | NR | NR | NR |
|  |  |  |  |  |  | HPR+150 mg clopidogrel  | CV death, MI or TVR | 1/36=3.1% |  |  | 0.09 comparing with the low rowlog-rank test  |  |  |  |
|  |  |  |  |  |  | HPR +75 mg clopidogrel  | CV death, MI or TVR | 5/38=16.4% |  |  |  |  |  |  |
| Marcucci, 2012{Marcucci, 2012 18217 /id}22390861ItalyNR | 600 mg clopidogrel loading dose followed by 75 mg daily doseASA IV 500 mg followed by 100-325 mg daily dose | LTA ADP | MACE | CV death , non-fatal MI | 6 months | HPRN=486 | CV death , non-fatal MI | NR | HR=2 | 1.2-3.4 | P=0.01(HPR vs no HPR)[Cox regression] | Yes (CV risk factors, renal failure, reducedejection fraction, multivessel disease, total stent length, bifurcation lesions, number of lesions treated, type of stent and use of GpIIb/IIIa inhibitors) | NR |  |
|  |  |  |  |  |  | No HPRN=701 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE | CV death , non-fatal MI | 7-12 months | HPRN=486 | CV death , non-fatal MI | NR | HR=2.7 | 1.4-5.3 | P=0.003(HPR vs no HPR)[Cox regression] | Yes (CV risk factors, renal failure, reducedejection fraction, multivessel disease, total stent length, bifurcation lesions, number of lesions treated, type of stent and use of GpIIb/IIIa inhibitors) | NR |  |
|  |  |  |  |  |  | No HPRN=701 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE | CV death , non-fatal MI | 12 months | HPRN=486 | CV death , non-fatal MI | NR | NR | NR | P<0.0001(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=701 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 carriers | CV death , non-fatal MI | 12 months | HPRN=144 | CV death , non-fatal MI | NR | NR | NR | P<0.0001(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=151 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 noncarriers | CV death , non-fatal MI | 12 months | HPRN=342 | CV death , non-fatal MI | NR | NR | NR | P<0.0001(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=550 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE | CV death , non-fatal MI | 6 months | HPRN=486 | CV death , non-fatal MI | NR | NR | NR | P<0.0001(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=701 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 carriers | CV death , non-fatal MI | 6 months | HPRN=144 | CV death , non-fatal MI | NR | NR | NR | P<0.006(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=151 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 noncarriers | CV death , non-fatal MI | 6 months | HPRN=342 | CV death , non-fatal MI | NR | NR | NR | P<0.007(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=550 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE | CV death , non-fatal MI | 7-12 months | HPRN=486 | CV death , non-fatal MI | NR | NR | NR | P=0.002(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=701 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 carriers | CV death , non-fatal MI | 7-12 months | HPRN=144 | CV death , non-fatal MI | NR | NR | NR | P=0.28(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=151 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 noncarriers | CV death , non-fatal MI | 7-12 months | HPRN=342 | CV death , non-fatal MI | NR | NR | NR | P<0.001(HPR vs no HPR)[log rank test] | No | NR |  |
|  |  |  |  |  |  | No HPRN=550 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE | CV death , non-fatal MI | 12 months | HPRN=486 | CV death , non-fatal MI | NR | AUC=0.66 | 0.6-0.71 | P<0.0001 | No | NR |  |
|  |  |  |  |  |  | No HPRN=701 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 carriers | CV death , non-fatal MI | 12 months | HPRN=144 | CV death , non-fatal MI | NR | AUC=0.64 | 0.57-0.71 | P<0.0001 | No | NR |  |
|  |  |  |  |  |  | No HPRN=151 | CV death, MI or TVR | NR |  |  |  |  |  |  |
|  |  |  | MACE in CYP2C19 noncarriers | CV death , non-fatal MI | 12 months | HPRN=342 | CV death , non-fatal MI | NR | AUC=0.64 | 0.57-0.71 | P<0.0001 | No | NR |  |
|  |  |  |  |  |  | No HPRN=550 | CV death, MI or TVR | NR |  |  |  |  |  |  |