**Appendix Table D14. Platelet reactivity during followup (discrete outcome)**

| **Author, year****UID****Country****Study name** | **Treatment** | **Genetic Test Used [index test]** | **Reactivity Outcome** | **Outcome Definition** | **Timing of measurement** | **Index test result: category (e.g., HPR+) – ONE ROW PER PHENOTYPE GROUP** | **Outcome status (e.g., HPR+ or HPR-)** | **No. with outcome status within phenotype group** | **Cut-off** | **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)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Giusti, 2007{Giusti, 2007 190 /id}18004210ItalyNR | LD:Clopidogrel 600 mg (orally) + 500 mg ASA (IV); MD: clopidogrel 75 mg and ASA 100 mg (both daily) | CYP2C19 \*2 | Aggregation with ADP 10 μmol/L | % maximal aggregation (discrete); cut-off based on previous literature | 24 h after PCI (6 d for patients receiving IIb/IIIa inhibitors) | \*2/\*2N = 40 | High RPR | 14 (35.0%) | ≥70% | NR | NR | P=0.002 (across 3 groups) [chi-square test] | NO | NO | Additional data in combination with AA as the agonist were not extracted (not agonist of interest to the report) |
|  |  |  |  |  |  | \*2/\*1N = 406[unclear why the sample size changed] |  | 85 (20.9%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1N = 973[unclear why the sample size changed] |  | 156 (16.0%) |  |  |  |  |  |  |  |
| Jinnai, 2009{Jinnai, 2009 120 /id}19531897JapanPartly industry funded | low-dose aspirin (81-100 mg/day) at enrollment; Clopidogrel LD= 300 mg on the first day + 75 mg/day MD. | CYP2C19 \*2, \*3 and \*1 | IPA | Change in platelet reactivity compared to baseline | 48h | PM = \*2/\*2 or \*2/\*3N = 6 | Responders | 1 | IPA ≥ 30% | NR | NR | NR | NR | NO | None |
|  |  |  |  |  |  | IM = \*2/\*1 or \*3/\*1N = 8  | Responders | 1 | IPA ≥ 30% |  |  |  |  |  |  |
|  |  |  |  |  |  | EM = \*1/\*1N = 11 | Responders | 7 | IPA ≥ 30% |  |  |  |  |  |  |
|  |  |  |  |  |  | PM = \*2/\*2 or \*2/\*3N = 6 | Hypo-responders | 3 | 10% ≤ IPA <30% |  |  |  |  |  |  |
|  |  |  |  |  |  | IM = \*2/\*1 or \*3/\*1N = 8  | Hypo -responders | 6 | 10% ≤ IPA <30% |  |  |  |  |  |  |
|  |  |  |  |  |  | EM = \*1/\*1N = 11 | Hypo -responders | 3 | 10% ≤ IPA <30% |  |  |  |  |  |  |
|  |  |  |  |  |  | PM = \*2/\*2 or \*2/\*3N = 6 | Non-responders | 2 | IPA < 10% |  |  |  |  |  |  |
|  |  |  |  |  |  | IM = \*2/\*1 or \*3/\*1N = 8  | Non-responders | 1 | IPA < 10% |  |  |  |  |  |  |
|  |  |  |  |  |  | EM = \*1/\*1N = 11 | Non-responders | 1 | IPA < 10% |  |  |  |  |  |  |
| Cuisset, 2011{Cuisset, 2011 18195 /id}21803320FranceNR | LD clopidogrel 600mgand aspirin 250mg, low responders received higher 150 mg MD clopidogrel | CYP2C19\*2(rs4244285) | PRI VASP | PRI VASP>50% as clopidogrel low response | after LD clopidogrel | CYP2C19\*2 carrier | low response | 46/86 | PRI VASP >50% | 46/86=53% | NR | 0.04chi-square test | NR | NR | NR |
|  |  |  |  |  |  | CYP2C19\*2 non carrier |  | 105/260 |  | 105/260=41% |  |  |  |  |  |
| Cuisset, 2011{Cuisset, 2011 18195 /id}21803320FranceNR | LD clopidogrel 600mgand aspirin 250mg, low responders received higher 150 mg MD clopidogrel | CYP2C19\*2(rs4244285) | PRI VASP | PRI VASP>50% as clopidogrel low response | 1 month | CYP2C19\*2 carrier | low response | NR | PRI VASP >50% | 9.5% | NR | <0.01chi-square test | NR | NR | NR |
|  |  |  |  |  |  | CYP2C19\*2 non carrier |  | NR |  | 15.7% |  |  |  |  |  |
| Frere, 2008{Frere, 2008 176 /id}18394438FranceNONE | 600 mg loading dose of clopidogrel + 250 mg aspirin  | CYP2C19 \*2 genotyping | ADP-induced reactivity by LTA | Measurement of ADP-stimulated aggregation | At the catheterization laboratory (≥12h after the loading dose) | \*2/\*2 | HPR + | 10 | >70% of baseline | NR | NR | 0.03 [using a recessive model for the prevalence of HPR+ among \*2/\*2 patients]0.03 [comparing the prevalence of HPR+ among \*2/\*1 patients; unclear genetic model] | NR | NO | Unclear reporting of statistical analyses but 2x3 data are adequate to reconstruct the analysis |
|  |  |  |  |  |  | \*2/\*2 | HPR - | 13 | <70% of baseline | NR | NR |  |  |  |  |
|  |  |  |  |  |  | \*2/\*1 | HPR + | 28 | >70% of baseline | NR | NR |  |  |  |  |
|  |  |  |  |  |  | \*2/\*1 | HPR - | 115 | <70% of baseline | NR | NR |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | HPR + | 110 | >70% of baseline | NR | NR |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | HPR - | 325 | <70% of baseline | NR | NR |  |  |  |  |
| Frere, 2009{Frere, 2009 117 /id}19496924FrancePart of larger observational study | 600 mg clopidogrel loading dose | CYP2C19 \*17 | VASP phosphorylation assay | Proportion of patients with PRI VASP >50% | After clopidogrel loading dose (exact timing NR) | \*17/\*17 and \*17/\*1(carriers vs. non-carriers)N = 214 | HPR+ = 50% HPR- = 50% | HPR+ = 107 HPR- = 107 | >50% vs. ≤50% | NR | NR | P=0.007 (carriers vs. non-carriers) [analysis method NR] | NO | NO | None |
|  |  |  |  |  |  | \*1/\*1N = 382 | HPR+ = 63%HPR- = 37% | HPR+ = 241HPR- = 141 |  |  |  |  |  |  |  |
| Bonello-Palot{Bonello-Palot, 2009 107 /id} 200919932784FranceNR | 600 mg clopidogrel LD | CYP2C19 \*2 | high on treatment platelet reactivity (HTPR) | Patients with a VASP index >50% | >6 to <12 hours after 600 mg clopidogrel LD | ≥ 1 CYP2C19\*2 allele (\*2/\*2 or Wild-type/\*2) | HTPR+ | 17/43 (39.5%) | VASP index >50% | Calculated DOR: 3.27 | 1.04, 10.2 | P=0.04 (≥ 1 CYP2C19\*2 allele vs wild-type) | NO | NR | None |
|  |  |  |  |  |  | Wild-type genotype (Wild-type/wild-type) | HTPR+ | 26/43 (60.5%) | VASP index >50% |  |  |  |  |  |  |
|  |  |  | Good responders | Patients with a VASP index <50% | >6 to <12 hours after 600 mg clopidogrel LD | ≥ 1 CYP2C19\*2 allele (\*2/\*2 or Wild-type/\*2) | HTPR- | 5/30 (16.7%) | VASP index <50% |  |  |  |  |  |  |
|  |  |  |  |  |  | Wild-type genotype (Wild-type/wild-type) | HTPR- | 25/30 (83.3%) | VASP index <50% |  |  |  |  |  |  |
|  | 600 mg loading dose (LD) of clopidogrel in good responders & 4 subsequent doses LD of of 600-mg clopidogrel  | CYP2C19 \*2 | Failed Dose adjustment | VASP reactivity <50% after 4 LD of 600 mg clopidogrel | >6 to <12 hours after 4th 600 mg clopidogrel LD | ≥ 1 CYP2C19\*2 allele (\*2/\*2 or Wild-type/\*2) | Failed dose+ | 3/10 (30%) | VASP index >50% | Calculated DOR: 0.99 | 0.23, 4.25 | P=0.01 (≥ 1 CYP2C19\*2 allele vs wild-type) | NO | NR | The data reported in the table and text is discrepant with the calculate values; for example the percentages reported in the text varies |
|  |  |  |  |  |  | Wild-type genotype (Wild-type/wild-type) | Failed dose+ | 7/10 (70%) | VASP index >50% |  |  |  |  |  |  |
|  |  |  | Successful Dose adjustment |  |  | ≥ 1 CYP2C19\*2 allele (\*2/\*2 or Wild-type/\*2) | Failed dose- | 19/63 (30.1%) | VASP index <50% |  |  |  |  |  |  |
|  |  |  |  |  |  | Wild-type genotype (Wild-type/wild-type) | Failed dose- | 44/63 (69.9%) | VASP index <50% |  |  |  |  |  |  |
| Harmsze 2010{Harmsze, 2010 102 /id}19934793NetherlandsNR | clopidogrel maintenance: 75 mg/day | CYP2C19\*2 | Poor responder | >70% aggregationusing 20 mmol/l ADP (LTA) | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | Poor responder + | 20% (N calculated as 59) | >70% aggregation | OR: 3.7 | 2.0,6.9 | P<0.001 (Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)) | NO | YES; false discovery ratetest (q value threshold 0.20) |  |
|  |  |  |  |  |  |  |  |  |  | OR: 3.8 | 2.0,7.2 | P<0.001 (Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)) | YES; adjusted for gender, age, BMI, DM, previous MI, days of clopidogrel administration before intervention, CYP3A4-metabolized statins, Ca+ channel blockers, PPI, SSRIs, and NSAIDs. | YES; false discovery ratetest (q value threshold 0.20) |  |
|  | clopidogrel maintenance: 75 mg/day | CYP2C19\*2 | Poor responder | PRU value greaterthan 235 (VerifyNow P2Y12 assay). | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | Poor responder + | NR | >235 PRU | OR: 2.8 | 1.6,5.0 | P<0.001 (Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)) | NO | YES; false discovery ratetest (q value threshold 0.20) |  |
|  |  |  |  |  |  |  |  |  |  | OR: 3.4 | 1.8,6.4 | P<0.001 (Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)) | YES; adjusted for gender, age, BMI, DM, previous MI, days of clopidogrel administration before intervention, CYP3A4-metabolized statins, Ca+ channel blockers, PPI, SSRIs, and NSAIDs. | YES; false discovery ratetest (q value threshold 0.20) |  |
|  | 300 mg clopidogrel loading dose | CYP2C19\*2 | Poor responder | >70% aggregationusing 20 mmol/l ADP (LTA) | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | Poor responder + | 40% according to LTA (N calculated as 52) | >70% aggregation | OR: 3.7 | 2.0,6.9 | P<0.001 (Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)) | NO | YES; false discovery ratetest (q value threshold 0.20) | Responder status as per PRU was not reported (unlike for the chronic clopidogrel group) |
|  |  |  |  |  |  |  |  |  |  | OR: 4.1 | 1.6,10.4 | P=0.003 (Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)) | YES; adjusted for gender, age, BMI, DM, previous MI, days of clopidogrel administration before intervention, CYP3A4-metabolized statins, Ca+ channel blockers, PPI, SSRIs, and NSAIDs. | YES; false discovery ratetest (q value threshold 0.20) |  |
| 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 loading dose + 75 mg/day clopidogrel (for 30 d w/ bare-metal stents or 6 mth w/ atleast 1 drug-eluting stent | CYP2C19 \*2 | High on-clopidogrel platelet reactivity | proportion of patients achieving an residual platelet aggregation >14% after stimulation with 5 μmol/l ADP | At PCI | Carriers (\*1/\*2 or \*2/\*2) | High on-clopidogrel platelet reactivity | 153/245 (62.4%) | 14% | OR=2.18 | 1.6,2.97 | P<0.001 (between carriers and noncarriers) | NO | NR |  |
|  |  |  |  |  |  | Noncarriers (\*1/\*1) | High on-clopidogrel platelet reactivity | 239/552(43.3%) | 14% |  |  |  |  |  |  |
|  |  |  |  |  | Pre-discharge | Carriers (\*1/\*2 or \*2/\*2) | High on-clopidogrel platelet reactivity | 97/235 (41.3%) | 14% | OR=2.43 | 1.74,3.38 | P<0.001 (between carriers and noncarriers) | NO | NR |  |
|  |  |  |  |  |  | Noncarriers (\*1/\*1) | High on-clopidogrel platelet reactivity | 118/525(22.5%) | 14% |  |  |  |  |  |  |
|  |  |  |  |  | At PCI | Carriers (\*1/\*2 or \*2/\*2) | High on-clopidogrel platelet reactivity | 153/245 (62.4%) | 14% | NR | NR | NR | YES; clinical characteristics (active smoker, BMI, hypertension, previous PCI), drug therapy(angiotensin-1 blockers, diuretics, oral antidiabetics), orAngiographic parameters (American Heart Association/American College of Cardiology coronary lesion type B2 orC, stenting in circumflex artery, vessel size, balloon size,minimal lumen diameter after PCI, stented length) | NR | OR was not reported; it can be estimate from digitizing Fig 1 & P value can be back calculated |
|  |  |  |  |  |  | Noncarriers (\*1/\*1) | High on-clopidogrel platelet reactivity | 239/552(43.3%) | 14% | NR | NR | NR |  |  |  |
|  |  |  |  |  | Pre-discharge | Carriers (\*1/\*2 or \*2/\*2) | High on-clopidogrel platelet reactivity | 97/235 (41.3%) | 14% | NR | NR | NR | YES; clinical characteristics (active smoker, BMI, hypertension, previous PCI), drug therapy(angiotensin-1 blockers, diuretics, oral antidiabetics), orAngiographic parameters (American Heart Association/American College of Cardiology coronary lesion type B2 orC, stenting in circumflex artery, vessel size, balloon size,minimal lumen diameter after PCI, stented length) | NR | OR was not reported; it can be estimate from digitizing Fig 1 & P value can be back calculated |
|  |  |  |  |  |  | Noncarriers (\*1/\*1) | High on-clopidogrel platelet reactivity | 118/525(22.5%) | 14% | NR | NR | NR |  |  |  |
| Hochholzer, 2010{Hochholzer, 2010 76 /id}20510210GermanyEXCELSIOR | clopidogrel | CYP2C19\* polymorphism  | Low response to clopidogrel | Residual platelet aggregation>14% | 2-4 hours after maintenance dose | CYP2C19\* polymorphism | Low response to clopidogrel  | 760 | Residual platelet aggregation>14% | OR=2.738 | 1.925-3.895 | <0.001 | Yes, age, arterial hypertension, diabetes mellitus,body mass index, platelets, ACE inhibition, nitrates, verapamil/diltiazem, previous balloon angioplasty, previous balloon angioplasty, previous CABG, impaired LV function, CCS angina class III or IV | NR | Figure 1 box and whisker plot |
|  | clopidogrel | CYP2C19\* polymorphism  | Low response to clopidogrel | Residual platelet aggregation after stimulation with 5 uM ADP | 2-4 hours after maintenance dose | CYP2C19\* polymorphism | Residual platelet aggregation | 760 | Residual platelet aggregation | Partial n2=0.052 | NR | <0.001 | Yes, age, arterial hypertension, diabetes mellitus,body mass index, platelets, ACE inhibition, nitrates, verapamil/diltiazem, previous balloon angioplasty, previous balloon angioplasty, previous CABG, impaired LV function, CCS angina class III or IV | NR |  |
| Jeong 2010{Jeong, 2010 70 /id}20650435KoreaNR | Clopidogrel | CYP2C19 | HPPR | See below | 2-4 hours | \*1/\*1 | HPPR+4(8.7) | 46 | 5uM ADP induced maximal platelet reactivity >50% | % | NR | 0.012 comparing the following row | NR | Yes  | Figure 3-6 bar graph of LTA and genotype |
|  |  |  |  |  |  | Rms | 23( 28.8) | 80 |  |  |  |  |  |  |  |
|  | clopidogrel | CYP2C19 | HPPR | See below | 2-4 hours | CYP2C19 variant | HPPR+ | 126 | 5uM ADP induced maximal platelet reactivity >50% | OR=4.237 | 1.362-13.158 | 0.013 | NO | NO |  |
|  | clopidogrel | CYP2C19 | HPPR | See below | 2-4 hours | CYP2C19 variant | HPPR+ | 126 | 5uM ADP induced maximal platelet reactivity >50% | OR=5.525 | 1.333-23.256 | 0.018 | Yes, CYP3A5\*3/\*3 carriers, carriage of ABCB1 variant, female sex, age(per 10 yr increment), BMI, ACS, current cmoking, hypertension, diabetes mellitus, chronic kidney disease, LV ejection fraction<45%, CYP3A4-metabolized statin, beta-blocker, calcium-channel blocker, nitrate, | NO |  |
| Bonello, 2010{Bonello, 2010 45 /id}20708365FranceNR | Clopidogrel  | CYP2C19  | HTPR | High on treatment platelet reactivity  | 12h | \*2 heterozygotes  | HTRP+ | 97/123 (77%) | VASP index ≥50% | Proportion | NR | <0.001 compared with row 2 and 3 | NR | NR |  |
|  | Clopidogrel  | CYP2C19  | HTPR | High on treatment platelet reactivity  | 12h | \*2 homozygotes  | HTPR+ | 6/11(54%) | VASP index ≥50% | Proportion | NR |  | NR | NR |  |
|  | Clopidogrel  | CYP2C19  | HTPR | High on treatment platelet reactivity  | 12h | Wild-type genotype  | HTPR+ | 154/277 (55.6) | VASP index ≥50% | proportion | NR |  | NR | NR |  |
|  | Clopidogrel  | CYP2C19  | HTPR | High on treatment platelet reactivity  | 12h | 2C19\*2 allele carriage  | HTPR+ | NR | VASP index ≥50% | OR=2.69 | 1.66-4.36 | <0.0001 | Yes, age, BMI | NR |  |
|  | Clopidogrel  | CYP2C19  | HTPR | High on treatment platelet reactivity  | 12h | No loss-of function allele | HTPR+ | 154/277 (55.6%) | VASP index ≥50% | NR | NR | NR | NR | NR |  |
|  | Clopidogrel  | CYP2C19  | HTPR | High on treatment platelet reactivity  | 3 additional 600-mg LDs | No loss-of function allele | HTPR+ | 137/154 (89%) | VASP index ≥50% | NR | NR | NR | NR | NR |  |
| Gurbel 2011{Gurbel, 2011 24 /id}21392617USANR | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 5uM ADP | \*2  | HRP + | 46% | 5 μM ADP 46% | Freqency  | NR | 0.015carriers vs noncarries | NR | NR |  |
|  |  |  |  |  |  | \*2 non carrier | HRP - | 25% |  |  | NR |   | NR | NR |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 20uM ADP | \*2 | HRP+ | 41% | 20 μM ADP 59% | Freqency  | NR | 0.013carriers vs noncarries | NR | NR |  |
|  |  |  |  |  |  | \*2 non carrier | HRP- | 18% |  |  | NR |  | NR | NR |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 5uM ADP | \*17 | HRP + | 27% | 5 μM ADP 46% | Freqency  | NR | 0.32carriers vs noncarries | NR | NR |  |
|  |  |  |  |  |  | \*17 non carrier | HRP - | 36% |  |  | NR |   | NR | NR |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 20uM ADP | \*17 | HRP+ | 14% | 20 μM ADP 59% | Freqency  | NR | 0.016carriers vs noncarries | NR | NR |  |
|  |  |  |  |  |  | \*17 non carrier | HRP- | 35% |  |  | NR |  | NR | NR |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 5uM ADP | \*2N=41 | HRP + | 15/27 | 5 μM ADP 46% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  | HRP- | 26/91 |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 5uM ADP | \*2 noncarrierN=77 | HRP + | 12/27 | 5 μM ADP 46% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  | HRP- | 65/91 |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 5uM ADP | \*17N=45 | HRP + | 8/27 | 5 μM ADP 46% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  | HRP- | 37/91 |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 5uM ADP | \*17N=73 | HRP + | 19/27 | 5 μM ADP 46% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  |  | 54/91 |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 20uM ADP | \*2N=41 | HRP + | 20/40 | 20 μM ADP 59% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  | HRP- | 21/78 |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 20uM ADP | \*2 noncarrierN=77 | HRP + | 20/40 | 20 μM ADP 59% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  | HRP- | 57/78 |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 20uM ADP | \*17N=45 | HRP + | 9/40 | 20 μM ADP 59% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  | HRP- | 36/78 |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19 | High platelet reactivity (HPR) | defined by specific cutoff values by ROC  | HPR 20uM ADP | \*17N=73 | HRP + | 31/40 | 20 μM ADP 59% | Count  | NR | NR | NR | NR |  |
|  |  |  |  |  |  |  | HRP- | 42/78 |  |  |  |  |  |  |  |
| Hwang 2011{Hwang, 2011 35 /id}21075428South KoreaNR | Clopidogrel  | CYP2C19\*2 | HRP | 5 umol/L ADP-MPA>50% | 12h | Codominant | HPR+34 | GG93 | 5 umol/L ADP-MPA>50% | Count | NR | 0.003 comparing the following 2 groups | NR | Yes |  |
|  |  |  |  |  |  |  | HPR-59 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*2 | HRP | 5 umol/L ADP-MPA>50% | 12h | Codominant | HPR+44 | GA79 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes |  |
|  |  |  |  |  |  |  | HPR-35 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*2 | HRP | 5 umol/L ADP-MPA>50% | 12h | Codominant | HPR+13 | AA18 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes  |  |
|  |  |  |  |  |  |  | HPR5 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*2 | HRP | 5 umol/L ADP-MPA>50% | 12h | dominant | HPR+34 | GG93 | 5 umol/L ADP-MPA>50% | Count | NR | 0.001 comparing the following group | NR | Yes |  |
|  |  |  |  |  |  |  | HPR59 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*2 | HRP | 5 umol/L ADP-MPA>50% | 12h | dominant | HPR+57 | GA/AA97 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes |  |
|  |  |  |  |  |  |  | HPR-40 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*2 | HRP | 5 umol/L ADP-MPA>50% | 12h | recessive | HPR+78 | GG/GA172 | 5 umol/L ADP-MPA>50% | Count | NR | 0.107 comparing the following group | NR | Yes |  |
|  |  |  |  |  |  |  | HPR-94 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*2 | HRP | 5 umol/L ADP-MPA>50% | 12h | recessive | HRP+13 | AA18 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes  |  |
|  |  |  |  |  |  |  | HPR-5 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*3 | HRP | 5 umol/L ADP-MPA>50% | 12h | Codominant | HRP+76 | GG165 | 5 umol/L ADP-MPA>50% | Count | NR | 0.008comparing the following 2 groups | NR | Yes  |  |
|  |  |  |  |  |  |  | HRP-88 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*3 | HRP | 5 umol/L ADP-MPA>50% | 12h | Codominant | HRP+15 | GA25 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes  |  |
|  |  |  |  |  |  |  | HRP-11 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*3 | HRP | 5 umol/L ADP-MPA>50% | 12h | Codominant | HRP+- | AA0 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes  |  |
|  |  |  |  |  |  |  | HRP-- |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*3 | HRP | 5 umol/L ADP-MPA>50% | 12h | dominant | HRP+76 | GG165 | 5 umol/L ADP-MPA>50% | Count | NR | 0.008comparing the following group | NR | Yes  |  |
|  |  |  |  |  |  |  | HRP-88 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*3 | HRP | 5 umol/L ADP-MPA>50% | 12h | dominant | HRP+15 | GA/AA25 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes  |  |
|  |  |  |  |  |  |  | HRP-11 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*3 | HRP | 5 umol/L ADP-MPA>50% | 12h | recessive | HRP+91 | GG/GA190 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes  |  |
|  |  |  |  |  |  |  | HRP-99 |  |  |  |  |  |  |  |  |
|  | Clopidogrel  | CYP2C19\*3 | HRP | 5 umol/L ADP-MPA>50% | 12h | recessive | HRP+- | AA0 | 5 umol/L ADP-MPA>50% | Count | NR |  | NR | Yes  |  |
|  |  |  |  |  |  |  | HRP-- |  |  |  |  |  |  |  |  |
| Kang, 2010{Kang, 2010 40 /id}20724801KoreaNR | clopidogrel | CYP2C19 | HPPR |  high post-treatment platelet reactivity | NR | Carrier of CYP2C19 varian | HPPR | 112/215  | 5 umol/L ADP-induced PRmax>50% | OR4.202 | 1.996-8.850 | <0.001 | Yes, sex, age, BMI, previous MI, previous stroke, current smoking, hypertension, diabetes mellitus, chronic kidney disease, LV ejection fraction<45%, CYP3A4-metabolized statin, beta blocker, angiotension blocker, calcium channel blocker, proton pump inhibitor | No  |  |
| Park 2011{Park, 2011 21 /id}21345843KoreaCILON-T | DAT | CYP2C19 | on-treatment platelet reactivity (High OPR) | on-treatment platelet reactivity (High OPR) | NR | Non-carrier | on-treatment platelet reactivity (High OPR) | 104 | NR | Odds ratio 1 | - | - | Yes. Age, gender, cigarette smoking, chronic kidney disease, antiplatelet treatment regimen according to CYP2C19 genotype | Yes  | Figure E multiple comparison |
|  | DAT | CYP2C19 | (High OPR | (High OPR | NR | Carrier  | (High OPR | 132 | NR | Odds ratio 2.93 | 1.64-5.21 | <0.001 | NR | NR |  |
|  | TAT | CYP2C19 | (High OPR | (High OPR | NR | Non-carrier | (High OPR | 87 | NR | Odds ratio 0.75 | 0.39-1.44 | 0.388 | NR | NR |  |
|  | TAT | CYP2C19 | (High OPR | (High OPR | NR | Carrier  | (High OPR | 151 | NR | Odds ratio 1.19 | 0.68-2.05 | 0.545 | NR | NR |  |
|  | Dual Clopidogrel  | CYP2C19 | OPR | on-treatment platelet reactivity  | NR | Non-carrier vsCarrier of  | on-treatment platelet reactivity  | CYP2C19 LOF allele236 | NR | N=104 for non carrierN=132 for carrier |  | Non-carrier vsCarrier of<0.001 | NR | NR |  |
|  | Triple Clopidogrel  | CYP2C19 | OPR | on-treatment platelet reactivity  | NR | Non-carrier vsCarrier of  | on-treatment platelet reactivity  | CYP2C19 LOF allele238 | NR | N=87 for non carrierN=151 for carrier |  | Non-carrier vsCarrier of0.139 | NR | NR |  |
|  | Dual Clopidogrel  | CYP2C19 | High OPR proportion | OPR >240 PRU  | NR | Non-carrier vsCarrier of  | OPR >240 PRU  | CYP2C19 LOF allele236 | OPR >240 PRU  | 37% for non carrier61% for carrier |  | Non-carrier vsCarrier <0.001 | NR | NR |  |
|  | Triple Clopidogrel  | CYP2C19 | High OPR proportion  | OPR >240 PRU | NR | Non-carrier vsCarrier of  | OPR >240 PRU | CYP2C19 LOF allele238 | OPR >240 PRU | 33% for non carrier44% for carrier |  | Non-carrier vsCarrier 0.115 | NR | NR |  |
|  | Dual and triple Clopidogrel  | CYP2C19 | OPR  | on-treatment platelet reactivity  | NR | Dual versus triple  | on-treatment platelet reactivity  | CYP2C19 LOF allele non carrier191 | NR | N=104 for dualN=87 for triple |  | Dual versus triple0.242 | NR | NR |  |
|  | Dual and triple Clopidogrel  | CYP2C19 | OPR  | on-treatment platelet reactivity  | NR | Dual versus triple  | on-treatment platelet reactivity  | CYP2C19 LOF allele carrier283 | NR | N=132 for dualN=151 for triple |  | Dual versus triple<0.001 | NR | NR |  |
|  | Dual and triple Clopidogrel  | CYP2C19 | High OPR proportion  | OPR >240 PRU | NR | Dual versus triple  | OPR >240 PRU | CYP2C19 LOF allele non carrier | OPR >240 PRU  | 37% for dual33% for triple |  | Dual versus triple0.241 | NR | NR |  |
|  | Dual and triple Clopidogrel  | CYP2C19 | High OPR proportion  | OPR >240 PRU | NR | Dual versus triple  | OPR >240 PRU | CYP2C19 LOF allele carrier | OPR >240 PRU | 61% for dual44% for triple |  | Dual versus triple<0.001 | NR | NR |  |
| Sibbing, 2010{Sibbing, 2010 48 /id}20492469GermanyNR | Clopidogrel  | CYP2C19 | Platelet aggregation  | Platelet aggregation  | NR | CYP2C19\*17  | Platelet aggregation  | 396 | >188Au\*min | 1.3 | 1.1-1.6 | \*17 vs no \*17 | no | no |  |
|  | Clopidogrel  | CYP2C19 | Platelet aggregation  | Platelet aggregation  | NR | CYP2C19\*17/\*17 | Platelet aggregation  |  | >188Au\*min | 1.7 | 1.1-2.7 | \*17/\*17 vs no \*17 | no | no |  |
|  | Clopidogrel  | CYP2C19 | Platelet aggregation | Platelet aggregation | NR | CYP2C19\*17  | Platelet aggregation | 396 | >188Au\*min | 1.4 | 1.1-1.7 | \*17 vs no \*17 | Yes, age, gender, smoking, diabetes mellitus, arterial hypertension, hypercholesterolemia, omeprazole/pantoprazole or ca2+ channel inhibition or phenprocouon, renal insufficiency, BMI,, fibrinogen levels. | no |  |
|  | Clopidogrel  | CYP2C19 | Platelet aggregation | Platelet aggregation | NR | CYP2C19\*17/\*17 | Platelet aggregation | 396 | >188Au\*min | 1.9 | 1.2-3.0 | \*17/\*17 vs no \*17 | Yes, age, gender, smoking, diabetes mellitus, arterial hypertension, hypercholesterolemia, omeprazole/pantoprazole or ca2+ channel inhibition or phenprocoumon, renal insufficiency, BMI,fibrinogen levels. | no |  |
| Bouman 2011{Bouman, 2011 9 /id}21628721NetherlandsGenetic substudy of the Popular study | Clopidogrel | CYP2C19 genetic test (real-time PCR) | High on-treatment platelet reactivity  | 5 umol/l ADP-induced LTA cutoff from ROC | Within 2 hr after blood sampling | \*1/\*1  | HPR+ | 38% of 737 patients | >42.9% aggregation | NR | NR | <0.001 vs. each of next two rows [chi-square test] | YES (age, sex, BMI, current smoking, systolic BP >140 mm Hg or diastolic BP >90 mm Hg, diabetes mellitus, LVEF <45%, renal failure (creatinine level >1.36 mg/dl), platelet count, mean platelet volue, clopidogrel regimen, PPI use, and amlodipine use) | NR | NONE |
|  |  |  |  |  |  | \*1/\*2 |  | 53% of 260 patients | >42.9% aggregation | NR | NR | 0.006 vs. next row |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 70% of 27 patients | >42.9% aggregation | NR | NR |  |  |  |  |
|  |  |  |  | 20 umol/l ADP-induced LTA cutoff from ROC |  | \*1/\*1  | HPR+ | 31% of 737 patients | >64.5% aggregation | NR | NR | <0.001 vs. each of next two rows | NR | NR | NR |
|  |  |  |  |  |  | \*1/\*2 |  | 52% of 260 patients | >64.5% aggregation | NR | NR | 0.013 vs. next row |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 78% of 27 patients | >64.5% aggregation | NR | NR |  |  |  |  |
|  |  |  |  | PlateletWorks assay cutoff from ROC |  | \*1/\*1  | HPR+ | 33% of 737 patients | > 80.5% aggregation | NR | NR | <0.001 vs. next row | NR | NR | NR |
|  |  |  |  |  |  | \*1/\*2 |  | 51% of 260 patients | > 80.5% aggregation | NR | NR | 0.045 vs. next row |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 91% of 27 patients | > 80.5% aggregation | NR | NR | 0.001 vs. first row |  |  |  |
|  |  |  |  | VerifyNow cutoff from ROC |  | \*1/\*1  | HPR+ | 34% of 737 patients | >236 PRU (P2Y12 reaction units) | NR | NR | <0.001 vs. each of next two rows | NR | NR | NR |
|  |  |  |  |  |  | \*1/\*2 |  | 49% of 260 patients | >236 PRU (P2Y12 reaction units) | NR | NR | 0.08 vs. next row |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 67% of 27 patients | >236 PRU (P2Y12 reaction units) | NR | NR |  |  |  |  |
|  |  |  | Risk of HPR | 5 umol/l ADP-induced LTA |  | \*1/\*2 vs.\*1/\*1 |  |  | >42.9% aggregation | Adjusted OR 1.80 | 1.28-2.54 | 0.001 [multivariate binary logistic regression] | NR | NR | NR |
|  |  |  |  | 20 umol/l ADP-induced LTA |  |  |  |  | >64.5% aggregation | Adjusted OR 2.53 | 1.78-3.60 | <0.001 [multivariate binary logistic regression] |  |  |  |
|  |  |  |  | Plateletworks assay |  |  |  |  | > 80.5% aggregation | Adjusted OR 1.96 | 1.24-3.09 | 0.004 [multivariate binary logistic regression] |  |  |  |
|  |  |  |  | VerifyNow P2Y12 |  |  |  |  | >236 PRU (P2Y12 reaction units) | Adjusted OR 2.14 | 1.50-3.07 | <0.001 [multivariate binary logistic regression] |  |  |  |
|  |  |  |  | 5 umol/l ADP-induced LTA |  | \*2/\*2 vs.\*1/\*1 |  |  | >42.9% aggregation | Adjusted OR 2.33 | 0.88-6.19 | 0.091 [multivariate binary logistic regression] |  |  |  |
|  |  |  |  | 20 umol/l ADP-induced LTA |  |  |  |  | >64.5% aggregation | Adjusted OR 4.54 | 1.61-12.80 | 0.004 [multivariate binary logistic regression] |  |  |  |
|  |  |  |  | Plateletworks assay |  |  |  |  | > 80.5% aggregation | Adjusted OR 12.92 | 1.52-109.98 | 0.019 [multivariate binary logistic regression] |  |  |  |
|  |  |  |  | VerifyNow P2Y12 |  |  |  |  | >236 PRU | Adjusted OR 2.63 | 0.97-7.14 | 0.059 [multivariate binary logistic regression] |  |  |  |
| Campo 2011{Campo, 2011 13 /id}21679849ItalyNR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| Fernando 2011{Fernando, 2011 233 /id}21696537AustraliaNR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| Geisler 2008{Geisler, 2008 161 /id}18781853GermanyNR | Clopidogrel | MassARRAY for \*2 | Residual platelet aggregation (RPA) | From turbidometry | Post-clopidogrel loading dose | \*1/\*1 | Low RPA | 144/175 patients with low RPA (82.3%) | RPA = or <47% at at least 6 hr after loading dose of clopidogrel | OR vs. \*1/\*2 + \*2/\*2, 4.6 | 2.5-8.7 | <0.0001 high RPA vs low RPAlogistic regression  | NR | NR | ORs and chi-square values are for having high RPA vs. low RPA among the three genotype subgroups |
|  |  |  |  |  |  |  | High RPA | 31//62 patients with high RPA (50%) | RPA >47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  | Clopidogrel | MassARRAY for \*2 | Residual platelet aggregation (RPA) | From turbidometry | Post-clopidogrel loading dose | \*1/\*2 | Low RPA | 28/175 (16%) | RPA = or <47% at at least 6 hr after loading dose of clopidogrel | Chi-square statistic vs. \*1/\*2 vs. \*2/\*2, 27.17 | NR | <0.001high RPA vs low RPAchi-square test | NR | NR | NR |
|  |  |  |  |  |  |  | High RPA | 24/62 (38.7%) | RPA >47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  | Clopidogrel | MassARRAY for \*2 | Residual platelet aggregation (RPA) | From turbidometry | Post-clopidogrel loading dose | \*2/\*2 | Low RPA | 3/175 (1.7%) | RPA = or <47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  |  |  |  |  |  |  | High RPA | 7/62 (11.3%) | RPA >47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  | Clopidogrel | MassARRAY for \*17 | Residual platelet aggregation (RPA) | From turbidometry | Post-clopidogrel loading dose | \*1/\*1 | Low RPA | 96/175 (54.9%) | RPA = or <47% at at least 6 hr after loading dose of clopidogrel | OR vs. \*1/\*17 + \*17/\*17, 0.62 | 0.34-1.14 | 0.14 high RPA vs low RPAlogistic regression | NR | NR | NR |
|  |  |  |  |  |  |  | High RPA | 41/62 (66.1%) | RPA >47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  | Clopidogrel | MassARRAY for \*17 | Residual platelet aggregation (RPA) | From turbidometry | Post-clopidogrel loading dose | \*1/\*17 | Low RPA | 65/175 (37.1%) | RPA = or <47% at at least 6 hr after loading dose of clopidogrel | Chi-square statistic vs. \*1/\*17 vs. \*17/\*17, 4.48 | NR | 0.11 high RPA vs low RPAchi square test | NR | NR | NR |
|  |  |  |  |  |  |  | High RPA | 14/62 (22.6%) | RPA >47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  |  |  |  |  |  | \*17/\*17 | Low RPA | 14/175 (8.0%) | RPA = or <47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  |  |  |  |  |  |  | High RPA | 7/62 (11.3%) | RPA >47% at at least 6 hr after loading dose of clopidogrel |  |  |  |  |  |  |
|  | Clopidogrel | MassARRAY for \*17 | Residual platelet aggregation (RPA) | From turbidometry | Post-clopidogrel loading dose | \*2 carriers | High RPA |  | RPA >47% at at least 6 hr after loading dose of clopidogrel | Chi-square statistic 21.31OR, 4.38 | 2.3-8.33 | <0.0001 high RPA vs low RPAlogistic regression  | yes[Multivariable logistic regression including age, diabetes status, LVEF, renal failure, ACS) | NR | NS for all other SNPs |
|  |  |  |  |  |  | One \*2 allele |  |  |  | OR 3.71 | 1.87-7.35 |  |  |  |  |
|  |  |  |  |  |  | Two \*2 alleles |  |  |  | OR 10.72 | 2.56-44.88 |  |  |  |  |
| Gurbel 2010{Gurbel, 2010 91 /id}19817997USA NR | 75 mg clopidogrel daily | TaqMan | HPR | Upper tertile of 5 uM ADP-induced platelet aggregation | NR | CYP2C19\*2 carrier | HPR+ | 13/17 | <43% | NR | NR | NR | NR | NO |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier |  | 4/19 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 carrier | 13/15 (NB the 13 is from text note that 75% of the 17 pts with HPR carried \*17) | **13/15** |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 4/21 | **4/21** |  |  |  |  |  |  |  |
|  |  |  | HPR | Upper tertile of 5 mM ADP-induced platelet aggregation | NR | CYP2C19\*17 noncarrier | 13/15 (NB the 13 is from text note that 75% of the 17 pts with HPR carried \*17) | **13/15** | <43% | NR | NR | NR | NR | NO | No |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 4/21 | **4/21** |  |  |  |  |  |  |  |
| Kim 2011{Kim, 2011 18 /id}21511217South KoreaCCELAMI2C19 | High-dose clopidogrel | PCR and SNaPshot assay kit | HPR | 20 mmol ADP-induced maximal platelet aggregation >59% | Predischarge | \*2 or \*3 noncarrier | Yes HPR | 11/24 (45.8%) | 20 mmol ADP-induced maximal platelet aggregation >59% | NR | NR | 0.666 vs. corresponiding cilostazol row below [chi-square statistics or Fisher exact test] | NR | NR | NONE |
|  |  |  |  |  |  | \*2 or \*3 carrier |  | 20/38 (52.6%) |  |  |  | 0.430 vs. corresponiding cilostazol row below [chi-square statistics or Fisher exact test] |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier |  | 2/24 (8.3%) |  |  |  | 0.235 vs. corresponiding cilostazol row below [chi-square statistics or Fisher exact test]Also P=0.002 vs next row [NR] |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier |  | 17/38 (44.7%) |  |  |  | 0.005 vs. corresponiding cilostazol row below [chi-square statistics or Fisher exact test] |  |  |  |
|  | High-dose clopidogrel | PCR and SNaPshot assay kit | HPR | high platelet reactivity  | Absolute change between baseline and 30 days | \*2 or \*3 noncarrier | HPR | 24 | NR | Mean 37.5% (SD NR) | NR | NR | NR | NR | Data also in Fig. 4 |
|  |  |  |  |  |  | \*2 or \*3 carrier |  | 38 | NR | Mean 7.9% (SD NR) | NR |  |  |  |  |
|  | Standar-dose clopidogrel + cilostazol |  |  |  | Pre-discharge | \*2 or \*3 noncarrier |  | 21/25 (52%) | NR | NR | NR | NR | NR | NR | NO |
|  |  |  |  |  |  | \*2 or \*3 carrier |  | 24/39 (61.5%) |  |  |  |  |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier |  | 0/25 (0%) | NR | NR | NR | P=0.174 vs. next row [NR] | NR | NR | no |
|  |  |  |  |  |  | \*2 or \*3 carrier |  | 6/39 (15.4%) |  |  |  |  |  |  |  |
|  |  |  |  | Absolute change between baseline and 30 days |  | \*2 or \*3 noncarrier |  | 25 | NR | Mean 54.2% (SD NR) |  |  |  |  | Data also in Fig. 4 |
|  |  |  |  |  |  | \*2 or \*3 carrier |  | 39 | NR | Mean 46.1% (SD NR) |  |  |  |  |  |
| Pettersen 2011{Pettersen, 2011 228 /id}21426546NorwayAspirin and Clopidogrel non-responsiveness clinical Endpoint Trial (ASCET) | Clopidogrel | TaqMan Drug Metabolism Assay | Clopidogrel resistance | per VASPPRI  | NR | \*2 carrier | Resistant | 46% | ≥ 55% PRI | NR | NR | < 0.001 vs. row below (either Student ’s unpaired t-test or Mann-Whitney U-test) | NR | NR | NONE |
|  |  |  |  |  |  | \*2 noncarrier | Resistant | 22% |  |  |  |  |  |  |  |
|  |  |  |  | Per VerifyNow PRU  |  | \*2 carrier | Resistant | 64 (54%) | ≥ 170 PRU |  |  | 0.003 vs. row below (either Student ’s unpaired t-test or Mann-Whitney U-test) |  |  |  |
|  |  |  |  |  |  | \*2 noncarrier | Resistant | 104 (22%) |  |  |  |  |  |  |  |
| Price, 201222624833USGIFT (Genotype Information and Functional Testing) Study—a prespeciﬁed genetic substudy of GRAVITAS (Gauging Responsiveness with A VerifyNow assay–Impact on Thrombosis And Safety) trial | Clopidogrel | MassARRAY and iPLEX | On-treatment platelet reactivity (OTR) | Per VerifyNow PRU | 12–24 hr after PCI (N=898 with data across clopidogrel doses, but total n=1008 apparently) | \*2 carrier | High OTR | NR | ≥ 230 PRU | R2 =  0.07 | NR | 2.2 x 10-15 | YESclinical covariates signiﬁcantly associated with OTR according to univariate analysis (age,sex, body mass index, current smoking, creatinine clearance<60 ml/min, diabetes mellitus, history of congestive heartfailure, hypertension, or hyperlipidemia) | NR | NONE |
|  |  |  |  |  |  | \*17 carrier | High OTR [apparently not low OTR here] | NR | ≥ 230 PRU | R2 =  0.005 | NR | 0.08 | YES, as above |  |  |
|  |  |  |  |  |  | Any 1 reduced-function CYP2C19 allele present in population (\*2, \*3, \*4, \*6, or \*8) [N=288] | High OTR | 200 | ≥ 230 PRU | OR 2.52 | 1.86-3.43 | NRVs. noncarriers (3 rows below) | YES, as above | NR | From Fig. 1a |
|  |  |  |  |  |  | Any 1 or 2 reduced-function CYP2C19 alleles present in population (\*2, \*3, \*4, \*6, or \*8) [N=317, overlapping with previous row] | High OTR | 223 | ≥ 230 PRU | 2.66 | 1.97-3.58 | NRVs. noncarriers (2 rows below) | YES, as above | NR | From Fig. 1a |
|  |  |  |  |  |  | Any 2 reduced-function CYP2C19 alleles present in population (\*2, \*3, \*4, \*6, or \*8) [N=29, overlapping with previous row] | High OTR | 23 | ≥ 230 PRU | 4.71 | 1.83-12.14 | NRVs. noncarriers (1 row below) | YES, as above |  | From Fig. 1a |
|  |  |  |  |  |  | Noncarriers of a reduced-function CYP2C19 allele [N=691] | High OTR | 346 | ≥ 230 PRU | NR | NR | NR | YES, as above |  | From Fig. 1a |
|  |  |  |  |  | 30 d after PCI (N=702 with data across all clopidogrel doses, although only 701 accounted for in this section) | \*2 carrier | High OTR | NR | ≥ 230 PRU | R2 =  0.10 | NR | 1.3 x 10-17 | YES, as above |  | NONE |
|  |  |  |  |  |  | \*17 carrier | “Reduced levels of OTR” | NR | < 230 PRU? | R2 =  0.022 | NR | 0.0004 | YES, as above |  |  |
|  |  |  |  |  |  | Any 1 reduced-function CYP2C19 allele present in population (\*2, \*3, \*4, \*6, or \*8) [N=235] | High OTR | 128 | ≥ 230 PRU | OR 2.29 | 1.59-3.30 | NRVs. noncarriers (3 rows below) | YES, as above |  | From Fig. 1b |
|  |  |  |  |  |  | Any 1 or 2 reduced-function CYP2C19 alleles present in population (\*2, \*3, \*4, \*6, or \*8) [N=256, overlapping with previous row] | High OTR | 145 | ≥ 230 PRU | 2.51 | 1.76-3.59 | NRVs. noncarriers (2 rows below) | YES, as above |  | From Fig. 1b |
|  |  |  |  |  |  | Any 2 reduced-function CYP2C19 alleles present in population (\*2, \*3, \*4, \*6, or \*8) [N=21, overlapping with previous row] | High OTR | 17 | ≥ 230 PRU | 9.51 | 2.86-31.63 | NRVs. noncarriers (1 row below) | YES, as above |  | From Fig. 1b |
|  |  |  |  |  |  | Noncarriers of a reduced-function CYP2C19 allele [N=445] | High OTR | 158 | ≥ 230 PRU | NR | NR | NR | YES, as above |  | From Fig. 1b |
|  |  |  |  |  | 6 mo after PCI (N=672 with data across all clopidogrel doses, although 676 noted in this section) | \*2 carrier | High OTR | NR | ≥ 230 PRU | R2 =  0.07 | NR | 1.9 x 10-11 | YES, as above | NR |  |
|  |  |  |  |  |  | \*17 carrier | “Reduced levels of OTR” | NR | < 230 PRU? | R2 =  0.015 | NR | 0.01 | YES, as above |  |  |
|  |  |  |  |  |  | Any 1 reduced-function CYP2C19 allele present in population (\*2, \*3, \*4, \*6, or \*8) [N=220] | High OTR | 111 | ≥ 230 PRU | OR 2.56 | 1.75-3.74 | NRVs. noncarriers (3 rows below) | YES, as above |  | From Fig. 1c |
|  |  |  |  |  |  | Any 1 or 2 reduced-function CYP2C19 alleles present in population (\*2, \*3, \*4, \*6, or \*8) [N=256, overlapping with previous row] | High OTR | 128 | ≥ 230 PRU | 2.80 | 1.93-4.07 | NRVs. noncarriers (2 rows below) | YES, as above |  | From Fig. 1a |
|  |  |  |  |  |  | Any 2 reduced-function CYP2C19 alleles present in population (\*2, \*3, \*4, \*6, or \*8) [N=21, overlapping with previous row] | High OTR | 16 | ≥ 230 PRU | 9.49 | 3.01-29.93 | NRVs. noncarriers (1 row below) | YES, as above |  | From Fig. 1b |
|  |  |  |  |  |  | Noncarriers of a reduced-function CYP2C19 allele [N=420] | High OTR | 130 | ≥ 230 PRU | NR | NR | NR | YES, as above |  | From Fig. 1a |
| Gremmel, 2012{Gremmel, 2012 18228 /id}22154242AustriaNR | Clopidogrel | Inﬁniti® CYP450 2C19+ assay | High on-treatmentresidual ADP-inducible platelet reactivity (HRPR)by LTA (n=286) | NR | 24 hr after PCI | Ultrarapid metabolizer (\*17/\*17 or wild type) [N=94] | HRPR (n=38) | 9 | > 67% for LTA | NR | NR | <0.05 for trend (this and next 3 rows) [Cochran-Armitage trend test] |  |  | NB: Absolute platelet reactivity data reported for metabolizer groups for each test in Fig. 1—could be digitized and reported as continuous platelet outcome in other table |
|  |  |  |  |  |  | Extensive metabolizer wild type/wild type) [N=105] |  | 12 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Intermediate metabolizer (\*2/\*17 or wild type or \*8/wild type) [N=84] |  | 16 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Poormetabolizer (\*2/\*2) [N=4] |  | 1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Carrier of LOF allele (\*2 or \*8) |  | 17 |  | OR 2.3 | 1.1-4.77 | NR(vs. next row) | Adjusted odds ratio for CYP2C19 \*2 carrier status as a predictor in multiple logistic regression with HRPR as dependen t variable |  |  |
|  |  |  |  |  |  | Noncarrier of LOF allele |  | 21 |  |  |  |  |  |  |  |
|  |  |  | HRPR by VerifyNow (n=287) |  |  | Ultrarapid metabolizer (\*17/\*17 or wild type) [N=94] | HRPR (n=102) | 26 | PRU > 235 for VerifyNow  |  |  | 0.02 for trend (this and next 3 rows) [Cochran-Armitage trend test] |  |  |  |
|  |  |  |  |  |  | Extensive metabolizer wild type/wild type) [N=106] |  | 39 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Intermediate metabolizer (\*2/\*17 or wild type or \*8/wild type) [N=83] |  | 34 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Poormetabolizer (\*2/\*2) [N=4] |  | 3 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Carrier of LOF allele (\*2 or \*8) |  | 37 |  | OR 1.6 | 0.9-2.8 | NR(vs. next row) | Adjusted odds ratio for CYP2C19 \*2 carrier status as a predictor in multiple logistic regression with HRPR as dependen t variable |  |  |
|  |  |  |  |  |  | Noncarrier of LOF allele |  | 65 |  |  |  |  |  |  |  |
|  |  |  | HRPR by VASP (n=284) |  |  | Ultrarapid metabolizer (\*17/\*17 or wild type) [N=94] | HRPR (n=139) | 38 | PRI > 50% for VASP |  |  | <0.01for trend (this and next 3 rows) [Cochran-Armitage trend test] |  |  |  |
|  |  |  |  |  |  | Extensive metabolizer wild type/wild type) [N=103] |  | 48 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Intermediate metabolizer (\*2/\*17 or wild type or \*8/wild type) [N=83] |  | 49 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Poormetabolizer (\*2/\*2) [N=4] |  | 4 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Carrier of LOF allele (\*2 or \*8) |  | 53 |  | OR 2.0 | 1.2-3.5 | NR(vs. next row) | Adjusted odds ratio for CYP2C19 \*2 carrier status as a predictor in multiple logistic regression with HRPR as dependen t variable |  |  |
|  |  |  |  |  |  | Noncarrier of LOF allele |  | 86 |  |  |  |  |  |  |  |
|  |  |  | HRPR by MEA (n=280) |  |  | Ultrarapid metabolizer (\*17/\*17 or wild type) [N=93] | HRPR (n=105) | 30 | AU ≥ 47 for MEA |  |  | 0.17 for trend (this and next 3 rows) [Cochran-Armitage trend test] |  |  |  |
|  |  |  |  |  |  | Extensive metabolizer wild type/wild type) [N=101] | ndgdhjfg | 39 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Intermediate metabolizer (\*2/\*17 or wild type or \*8/wild type) [N=82] |  | 34 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Poormetabolizer (\*2/\*2) [N=4] |  | 2 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Carrier of LOF allele (\*2 or \*8) |  | 36 |  | OR 1.4 | 0.8-2.4 | NR(vs. next row) | Adjusted odds ratio for CYP2C19 \*2 carrier status as a predictor in multiple logistic regression with HRPR as dependen t variable |  |  |
|  |  |  |  |  |  | Noncarrier of LOF allele  |  | 69 |  |  |  |  |  |  |  |
|  |  |  | HRPR by Impact-R (n=280) |  |  | Ultrarapid metabolizer (\*17/\*17 or wild type) [N=93] | HRPR (n=121) | 38 | SC<3% for Impact-R |  |  | <0.1 for trend (this and next 3 rows) [Cochran-Armitage trend test] |  |  |  |
|  |  |  |  |  |  | Extensive metabolizer wild type/wild type) [N=101] |  | 39 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Intermediate metabolizer (\*2/\*17 or wild type or \*8/wild type) [N=82] |  | 40 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Poormetabolizer (\*2/\*2) [N=4] |  | 4 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Carrier of LOF allele (\*2 or \*8) |  | 44 |  | OR 1.6 | 0.9-2.7 | NR(vs. next row) | Adjusted odds ratio for CYP2C19 \*2 carrier status as a predictor in multiple logistic regression with HRPR as dependen t variable |  |  |
|  |  |  |  |  |  | Noncarrier of LOF allele  |  | 77 |  |  |  |  |  |  |  |
| Tello-Montoliu 2012{Tello-Montoliu, 2012 18200 /id}22116003Spainstudy one of the paper | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*2 | LTA ADP platelet aggregationHigh on-clopidogrel platelet reactivity(HOPR) | LTA ADP 5uM | in hospital | G/G 31 | HOPR+ | 18 (58.1) | >=46% | chi-square test | NR | NR | 0.091comparing with the next row | NR | NR |
|  |  |  |  |  |  | \*/A 9 |  | 8(88.9) |  |  |  |  |  |  |  |
|  | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*2 | VASP ADP High on-clopidogrel platelet reactivity(HOPR) | VASP ADP | in hospital | G/G31 | HOPR+ | 20 (64.5) | >=50% | chi-square test | NR | NR | 0.036comparing with the next row | NR | NR |
|  |  |  |  |  |  | \*/A 9 |  | 9 (100) |  |  |  |  |  |  |  |
| Tello-Montoliu 2012{Tello-Montoliu, 2012 18200 /id}22116003Spainstudy one of the paper | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*17 | LTA ADP platelet aggregationHigh on-clopidogrel platelet reactivity(HOPR) | LTA ADP 5uM | in hospital | C/C 27 | HOPR+ | 20 (74.1) | >=46% | chi-square test | NR | NR | 0.084comparing with the next row | NR | NR |
|  |  |  |  |  |  | \*/T 13 |  | 6 (46.2) |  |  |  |  |  |  |  |
|  | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*17 | VASP ADP High on-clopidogrel platelet reactivity(HOPR) | VASP ADP | in hospital | C/C 27 | HOPR+ | 22 (81.5) | >=50% | chi-square test | NR | NR | 0.074comparing with the next row | NR | NR |
|  |  |  |  |  |  | \*/T 13 |  | 7 (53.9) |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Tello-Montoliu 2012{Tello-Montoliu, 2012 18200 /id}22116003Spainstudy one of the paper | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*2 and \*17 | LTA ADP platelet aggregationHigh on-clopidogrel platelet reactivity(HOPR) | LTA ADP 5uM | in hospital | \*2 G/G\*17 C/Cn=19 | HOPR+ | 13 (68.4) | >=46% | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | \*2 \*/A\*17 C/Cn=8 |  | 7(87.5) | >=46% |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 G/G\*17 \*/Tn=12 |  | 5 (41.7) | >=46% |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 \*/A\*17 \*/Tn=1 |  | 1(100) | >=46% |  |  |  |  |  |  |
|  | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*2 | VASP ADP High on-clopidogrel platelet reactivity(HOPR) | VASP ADP | in hospital | \*2 G/G\*17 C/Cn=19 | HOPR+ | 14 (73.7) | >=50% | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | \*2 \*/A\*17 C/Cn=8 |  | 8 (100) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 G/G\*17 \*/Tn=12 |  | 6 (50) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 \*/A\*17 \*/Tn=1 |  | 1(100) |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Harmsze, 2011{Harmsze, 2011 18201 /id}21854540NetherlandsPOPular | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI-, \*2 - | HOPR+ | NR | NR | OR=1.7 | 1.0-2.7 | 0.03 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI-, \*2 - | HOPR+ | NR | NR | OR=1.6 | 0.97-2.6 | NR | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB-, PPI+, \*2 - | HOPR+ | NR | NR | OR=1.6 | 1.0-2.8 | 0.045compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB-, PPI+, \*2 - | HOPR+ | NR | NR | OR=1.5 | 1.0-2.6 | 0.035 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 - | HOPR+ | NR | NR | OR=4.1 | 2.0-8.4 | <0.0001 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 - | HOPR+ | NR | NR | OR=3.2 | 1.5-6.9 | 0.002 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB-, PPI-, \*2+ | HOPR+ | NR | NR | OR=2.8 | 1.8-4.4 | <0.0001 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB-, PPI-, \*2 + | HOPR+ | NR | NR | OR=3.1 | 1.9-4.9 | <0.0001 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB-, PPI+, \*2+ | HOPR+ | NR | NR | OR=3.3 | 1.4-7.9 | 0.006 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB-, PPI+, \*2 + | HOPR+ | NR | NR | OR=3.0 | 1.3-7.4 | 0.014 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI-, \*2+ | HOPR+ | NR | NR | OR=4.5 | 2.4-8.6 | <0.0001 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI-, \*2 + | HOPR+ | NR | NR | OR=4.4 | 2.3-8.7 | <0.0001 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI+, \*2+- | HOPR+ | NR | NR | OR=2.6 | 0.76-8.6 | 0.13 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 5uM | LTA ADP high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 + | HOPR+ | NR | NR | OR=2.4 | 0.68-8.2 | 0.18 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Harmsze, 2011{Harmsze, 2011 18201 /id}21854540NetherlandsPOPular | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI-, \*2 - | HOPR+ | NR | NR | OR=1.8 | 1.1-2.8 | 0.016 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI-, \*2 - | HOPR+ | NR | NR | OR=1.6 | 1.0-2.6 | 0.019 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB-, PPI+, \*2 - | HOPR+ | NR | NR | OR=2.1 | 1.2-3.6 | 0.006 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB-, PPI+, \*2 - | HOPR+ | NR | NR | OR=1.8 | 1.0-3.1 | 0.05 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 - | HOPR+ | NR | NR | OR=3.3 | 1.6-6.7 | 0.001 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 - | HOPR+ | NR | NR | OR=2.4 | 1.2-5.2 | 0.021 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB-, PPI-, \*2+ | HOPR+ | NR | NR | OR=2.2 | 1.4-3.4 | 0.001 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB-, PPI-, \*2 + | HOPR+ | NR | NR | OR=2.3 | 1.4-3.6 | 0.001 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB-, PPI+, \*2+ | HOPR+ | NR | NR | OR=4.3 | 1.8-10.4 | 0.001 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB-, PPI+, \*2 + | HOPR+ | NR | NR | OR=3.1 | 1.3-7.8 | 0.014 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI-, \*2+ | HOPR+ | NR | NR | OR=3.4 | 1.8-6.4 | <0.0001 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI-, \*2 + | HOPR+ | NR | NR | OR=3.2 | 1.7-6.2 | <0.0001 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI+, \*2+- | HOPR+ | NR | NR | OR=7.4 | 1.9-28.6 | 0.004 compared with non-drug and non CYP2C19 \*2 carriers | NR | NR | NR |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+aspirin 80-100 mg day | CYP2C19 \*2 | verify now P2Y12 | verify now P2Y12high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 + | HOPR+ | NR | NR | OR=6.7 | 1.7-27.4 | 0.008 compared with non-drug and non CYP2C19 \*2 carriers | yes, gender, age, BMI, renal function, clopidogrel loading dose, smoking, DM, LVEF<45% | NR | NR |
| Aleil, 2009{Aleil, 2009 18222 /id}19624462FranceVASP-02 [genetic reanalysis thereof] | 75 (n=95) or 150 (n=58) mg/day clopidogrel | VASP | High platelet reactivity (>69% PRI) at baseline | NR | Baseline (before clopidogrel receipt) | \*2 carrier (\*2/wild type or \*2/\*2) (n=37) | High PRI (poor response) | 16 (42%) overall (10 receiving 150 mg and 6 receiving 75 mg) | >69% | 3.393 | 1.062-10.841 | P=0.039 [multivariate logistic regression] | NR | NR | Table 2 shows continuous PRI data but it’s by dose level and N’s are not given, so not extracted |
|  |  |  |  |  |  | \*2 noncarrier (wild type/wild type) (n=116) | High PRI (poor response) | 26 (22%) overall (NR by dose level) |  |  |  |  |  |  |  |
| Mega, 2011{Mega, 2011 18190 /id}22088980USAELEVATE-TIMI 56 | 75 mg clopidogrel daily | Pyrosequencing and Nanosphere Verigene | Response to clopidogrel | On-treatment platelet reactivity by VerifyNow | Any time within 2-week treatment period for this dose | \*1/\*1 (N=234) | Nonresponse | 53 (23%) | >=230 PRU | NR | NR | NR | NR | NR | NONE |
|  |  |  |  |  |  | \*2/\*1 (N=76) |  | 40 (52%) |  |  |  | <0.001 vs. corresponding count for 150 mg dose (2 rows below) [GLM] |  |  |  |
|  | 150 mg clopidogrel daily |  |  |  |  | \*1/\*1 (N=227) |  | 28 (12%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (N=73) |  | 27 |  |  |  | 0.002 vs. next row [GLM] |  |  | This datum estimated visually by extractor from Fig 3 (above and below data were given in text; only this datum was not) |
|  | 225 mg clopidogrel daily |  |  |  |  | \*2/\*1 (N=75) |  | 8 (10%) |  |  |  | 0.90 vs. next row [GLM] |  |  |  |
|  | 300 mg clopidogrel daily |  |  |  |  | \*2/\*1 (N=73) |  | 7 (10%) |  |  |  |  |  |  |  |
| Kim, 2011{Kim, 2012 18236 /id}KoreaACCEL-TRIPLE | cilostazol 100 mg twice a dayclopidogrel 75 mg once a dayaspirin 200mg once a day | CYP2C19  | HPR5uM ADP agg MAX(%)>46% | HPR5uM ADP agg MAX>(%) | 30 days | EM | 48 | 3(6.3) | >46% | NR | NR | 0.099chi square test | NR | NR | NR |
|  |  |  |  |  |  | IM | 54 | 4(7.4) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | PM | 25 | 5 (20) |  |  |  |  |  |  |  |
| Bonello, 2012{Bonello, 2012 18189 /id}22285300FranceNR | oral LD: 600 mg clopidogrel and 250 mg aspirin | CYP2C19 \*2 | VASP | high on-treatment platelet reactivity(HTPR) by VASP>50% | <24 hrs after clopidogrel LD | Carriers of atleast one \*2 allele (wt /\*2 or \*2/\*2)N=106 | HPR+ | 75 | VASP PRI >50% | OR (calculated)=1.762 | 1.056-2.95[calculated] | p=0.015 (reported); p=0.024 (calculated)(carriers of \*2 vs wild-type allele)[Chi-square] | No | NR |  |
|  |  |  |  |  |  | Carriers of atleast one \*2 allele (wt /\*2 or \*2/\*2)N=106 | HPR- | 31 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | wild-type (wt) / wild-type (wt)N=261 | HPR+ | 151 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | wild-type (wt) / wild-type (wt)N=261 | HPR- | 110 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Carriers of atleast one \*2 allele (wt /\*2 or \*2/\*2)N=106 | HPR+ | 75 | VASP PRI >50% | OR=1.81  | 1.09-3.01 | p=0.02(carriers of \*2 vs wild-type allele)[logistic regression] | Yes; age. BMI | NR |  |
|  |  |  |  |  |  | Carriers of atleast one \*2 allele (wt /\*2 or \*2/\*2)N=106 | HPR- | 31 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | wild-type (wt) / wild-type (wt)N=261 | HPR+ | 151 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | wild-type (wt) / wild-type (wt)N=261 | HPR- | 110 |  |  |  |  |  |  |  |
| Hochholzer, 2011{Hochholzer, 2011 18208 /id}21884870NREXCELSIOR | LD of 600 mg of clopidogrel prior to PCI. After PCI, MD of aspirin (≥100 mg/d) and clopidogrel (75 mg/d) for 30 days (bare-metal stents) or 6 months (at least 1 drug-eluting stent) | CYP2C19 \*2 | LTA | Residual platelet aggregation ≥14% | 24 hrs | CYP2C19 \*2 carrier | High on-tx platelet reactivity | NR | 14% | OR= 2.90 | NR | <0.001 (carrier vs non carrier) [logistic regression] | Yes | NR |  |
|  |  |  |  |  |  | Non CYP2C19 \*2 carrier | High on-tx platelet reactivity | NR | 14% |  |  |  |  |  |  |
| Siller-matula, 2012{Siller-Matula, 2012 1 /id}22260716AustriaPEGASUS-PCI | clopidogrel LD 600mg, MD 75mg | CYP2C19 \*2 | MEA | <48U | 12 months | LOF allele (CYP2C19\*2)N=123 | MEA<48U | 90 | 48 | OR= 0.57 | 0.3418 to 0.9397 | P=0.027 (carrier vs non carrier) [chi square test] | Yes | NR |  |
|  |  |  |  |  |  |  | MEA>48U | 33 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | No LOF allele (CYP2C19\*1)N=278 | MEA<48U | 231 |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  | MEA>48U | 48 |  |  |  |  |  |  |  |
| Kassimis, 2012{Kassimis, 2012 18209 /id}21831410GreeceNR | No clopidogrel LD for those on 75 mg/d MD; LD 600 mg before PCI (if no and <7 days pretreatment)Post PCI: Clopidogrel MD 75 mg/d and aspirin 100 mg/d | CYP2C19\*2 | Aggregation by VerifyNow | Aggregation by VerifyNow | 24-48 hours after procedure | CYP2C19\*2 CarriersN=38 | High on-treatmen platelet reactivityPRU>235 | NR | 235 | OR=3.02 | 1.16-7.86 | P=0.023(carrier vs non carrier)[linear mixed maximumlikelihood model] | no | nr |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarriersN=108 |  | NR |  |  |  |  |  |  |  |
|  |  | CYP2C19\*17 | Aggregation by VerifyNow | Aggregation by VerifyNow | 24-48 hours after procedure | CYP2C19\*17 CarriersN=nr | High on-treatmen platelet reactivityPRU>235 | NR | 235 | OR=1.95 | 0.85-4.44 | P=0.1(carrier vs non carrier)[linear mixed maximumlikelihood model] | no | nr |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarriersN=nr |  | NR |  |  |  |  |  |  |  |
| Namazi, 2012{Namazi, 2012 18206 /id}22265638IranNR | Clopidogrel LD: 600 mg Clopidogrel MD: 150 mg/day for two weeks and 75 mg/day for 12 monthsAspirin 80 mg/d | CYP2C19 \*2 and \*3 | Clopidogrel Nonresponsiveness by LTA | Platelet inhibition <10% | 24-48 hours after procedure | Carriers of CYP2C19 \*2 and \*3 alleleN=12 | Clopidogrel Nonresponsiveness by LTA | NR | IPA<10% | NR | NR | P>0.05(carrier \*2/\*3 vs carrier \*1)[Fisher’s test] | no | nr |  |
|  |  |  |  |  |  | Carriers of CYP2C19 \*1 alleleN=100 |  | NR |  |  |  |  |  |  |  |
| Rideg, 2011{Rideg, 2011 18210 /id}21806387HungaryDOSER | LD: 600 mg clopidogrel & 300 mg aspirinRandomized to 4 weeks of 75 or 150 mg clopidogrelMD: 75 mg clopidogrel/day | CYP2C19 \*1, \*2, \*3 and \*17 | LTA - High on treatment platelet reactivity | >46% | 24 hours | GOF/GOF | HTPR | 28 | 46 | NR (Prevalence of HTPR from Fig1b) | NR | P=0.05Between all groups[Kruskal-wallis test] |  |  |  |
|  |  |  |  |  |  | Wt/GOF |  | 41 |  | NR (Fig 1b) |  |  |  |  |  |
|  |  |  |  |  |  | Wt/wt |  | 75 |  | NR (Fig 1b) |  |  |  |  |  |
|  |  |  |  |  |  | Wt/LOFGOF/LOF |  | 41 |  | NR (Fig 1b) |  |  |  |  |  |
|  |  |  |  |  |  | LOF/LOF |  | 4 |  | NR (Fig 1b) |  |  |  |  |  |
| Rideg, 2011{Rideg, 2011 18210 /id}21806387HungaryDOSER | LD: 600 mg clopidogrel & 300 mg aspirinRandomized to 4 weeks of 75 or 150 mg clopidogrelMD: 75 mg clopidogrel/day | CYP2C19 \*1, \*2, \*3 and \*17 | LTA - High on treatment platelet reactivity | >46% | 24 hours | LOF carrier (\*1\*2 or \*2\*2) | HTPR | 31 | 46% | OR=3.35 | 1.27-8.86 | P=0.02(LOF carrier vs noncarrier)[logistic regression] | no | nr |  |
|  |  |  |  |  |  | Non LOF carrier  |  | 158 |  |  |  |  |  |  |  |
| Rideg, 2011{Rideg, 2011 18210 /id}21806387HungaryDOSER | LD: 600 mg clopidogrel & 300 mg aspirinRandomized to 4 weeks of 75 or 150 mg clopidogrelMD: 75 mg clopidogrel/day | CYP2C19 \*1, \*2, \*3 and \*17 | LTA - High on treatment platelet reactivity | >46% | 24 hours | LOF carrier (\*1\*2 or \*2\*2) | HTPR | 31 | 46% | OR=3.67 | 1.34-9.99 | P=0.01(LOF carrier vs noncarrier)[logistic regression] | yes | nr |  |
|  |  |  |  |  |  | Non LOF carrier  |  | 158 |  |  |  |  |  |  |  |
| Rideg, 2011{Rideg, 2011 18210 /id}21806387HungaryDOSER | LD: 600 mg clopidogrel & 300 mg aspirinRandomized to 4 weeks of 75 or 150 mg clopidogrelMD: 75 mg clopidogrel/day | CYP2C19 \*1, \*2, \*3 and \*17 | LTA - High on treatment platelet reactivity | >46% | 24 hours | GOF carrier (\*1\*17 or \*17\*17) | HTPR | 4 | 46% | OR=9.82 | 1.3-74.23 | P=0.03(LOF carrier vs noncarrier)[logistic regression] | no | nr |  |
|  |  |  |  |  |  | Non homozygote LOF carrier |  | 185 |  |  |  |  |  |  |  |
| Rideg, 2011{Rideg, 2011 18210 /id}21806387HungaryDOSER | LD: 600 mg clopidogrel & 300 mg aspirinRandomized to 4 weeks of 75 or 150 mg clopidogrelMD: 75 mg clopidogrel/day | CYP2C19 \*1, \*2, \*3 and \*17 | LTA - High on treatment platelet reactivity | >46% | 24 hours | GOF carrier (\*1\*17 or \*17\*17) | HTPR | 83 | 46% | OR=0.56 | 0.2-1.54 | P=0.26(LOF carrier vs noncarrier)[logistic regression] | no | nr |  |
|  |  |  |  |  |  | Non GOF carrier  |  | 106 |  |  |  |  |  |  |  |
| Rideg, 2011{Rideg, 2011 18210 /id}21806387HungaryDOSER | LD: 600 mg clopidogrel & 300 mg aspirinRandomized to 4 weeks of 75 or 150 mg clopidogrelMD: 75 mg clopidogrel/day | LOF+GOF+ABCB1 | LTA - High on treatment platelet reactivity | >46% | 24 hours | LOF+GOF+ABCB1 | HTPR | NR | 46% | AUC=0.697 | 0.558-0.837 | P=0.006(LOF+GOF+ABCB1 vs non LOF+GOF+ABCB1)[ROC curve] | no | nr |  |
|  |  | LOF+GOF | LTA - High on treatment platelet reactivity | >46% | 24 hours | LOF+GOF | HTPR | 128 | 46% | AUC=0.677 | 0.538-0.802 | P=0.018(LOF+GOF vs non LOF+GOF)[ROC curve] | no | nr |  |
|  |  | LOF | LTA - High on treatment platelet reactivity | >46% | 24 hours | LOF | HTPR | 45 | 46% | AUC=0.639 | 0.495-0.783 | P=0.053(LOF+GOF vs non LOF+GOF)[ROC curve] | no | nr |  |
| Jeong, 2011{Jeong, 2011 18207 /id}22045970KoreaNR | LD: 600 mg clopidogrel & 300 mg aspirinMD: 75 mg/d clopidogrel & aspirin 200 mg/d for 1 month and 100-200 mg/day for 1 year | CYP2C19 \*1, \*2, and \*3  | LTA - High on treatment platelet reactivity | >59% | 3 days | 1/\*1N=104  | HPR | 45 (43.3%)  | 59% | OR=1.96  | 0.88–4.37 | P=0.091(One LOF allele carriage vs no carriage)[regression] | no | yes |  |
|  |  |  |  |  |  | \*1/\*2 N=98 |  | 50 (51.0%) |  | OR=1.83  | 0.80–4.17 | P=0.152(One LOF allele carriage vs no carriage)[regression] | Yes | yes |  |
|  |  |  |  |  |  | \*1/\*3 N=30 |  | 16 (53.3%) |  | OR=2.74 | 1.21–6.21 | P=0.015(two LOF allele carriage vs no carriage)[regression] | No | yes |  |
|  |  |  |  |  |  | \*2/\*2 N=20 |  | 13 (65.0%) |  | OR=2.81 | 1.21–6.54 | P=0.016(two LOF allele carriage vs no carriage)[regression] | Yes | yes |  |
|  |  |  |  |  |  | \*2/\*3N=14 |  | 10 (71.4%) |  |  |  |  |  |  |  |
| Collet, 2011{Collet, 2011 18192 /id}21511218FranceCLOVIS-2 | LD: Clopidogrel 300 or 900 mgMD: Aspirin 75 mg/d and/or clopidogrel 75 mg and | CYP2C19\*2 | LTA | High On-Treatment Platelet Reactivity (MPA >64.5%) | baseline | wt/wt | HPR | 7/52 (13.46%) | NR | NR | NR | P=0.34[between CYP2C19 \*2 genotypes][kruskall wallis test] |  |  |  |
|  |  |  |  |  |  | wt/\*2 |  | 7/31 (22.6%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 1/3 (33.3%)  |  |  |  |  |  |  |  |
|  |  |  |  |  | 300 mg post loading | wt/wt | HPR | 3/58 (5.17%) | NR | NR | NR | P=0.0017[between CYP2C19 \*2 genotypes][kruskall wallis test] |  |  |  |
|  |  |  |  |  |  | wt/\*2 |  | 6/41 (14.63%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 4/7 (57.14%) |  |  |  |  |  |  |  |
|  |  |  |  |  | 900 mg post loading | wt/wt | HPR | 2/58 (3.45%) | NR | NR | NR | P=0.005[between CYP2C19 \*2 genotypes][kruskall wallis test] |  |  |  |
|  |  |  |  |  |  | wt/\*2 |  | 2/41 (4.88%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 4/7 (51.14%) |  |  |  |  |  |  |  |
|  |  |  | VerifyNow | High On-Treatment Platelet Reactivity (PRU >235) | baseline | wt/wt | HPR | 3/52 (5.77%) | NR | NR | NR | P=0.081[between CYP2C19 \*2 genotypes][kruskall wallis test] |  |  |  |
|  |  |  |  |  |  | wt/\*2 |  | 5/31 (16.13%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 1/3 (33.3%) |  |  |  |  |  |  |  |
|  |  |  |  |  | 300 mg post loading | wt/wt | HPR | 2/58 (3.45%) | NR | NR | NR | P=0.348[between CYP2C19 \*2 genotypes][kruskall wallis test] |  |  |  |
|  |  |  |  |  |  | wt/\*2 |  | 1/41 (2.44%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 1/7 (14.29%) |  |  |  |  |  |  |  |
|  |  |  |  |  | 900 mg post loading | wt/wt | HPR | 1/58 (1.72%) | NR | NR | NR | P=0.242[between CYP2C19 \*2 genotypes][kruskall wallis test] |  |  |  |
|  |  |  |  |  |  | wt/\*2 |  | 1/41 (2.44%) |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 1/7 (14.29%) |  |  |  |  |  |  |  |
| Hulot, 2011{Hulot, 2011 18321 /id}21972404 FranceCLOVIS-2 | LD 300 or 900 mg clopidogrel | CYP2C19\*2 | high on-treatment platelet reactivity | maximalplatelet aggregation >59% | 6 hrs | \*1/\*1 | HPR+ | 55 | 59% | NR | NR | NR | NR | NR | “Multivariate analyses using maximal platelet aggregation or high ontreatment platelet reactivity as dependent variables lead to same result (CYP2C19\*2 carriage remained the only significant predictor of platelet function response to clopidogrel LD irrespective of the platelet function assay (P<0.001 for both loading doses))” |
|  |  |  |  |  |  | \*1/\*2 |  | 41 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 |  | 7 |  |  |  |  |  |  |  |