**Appendix Table D15. Platelet reactivity during followup (continuous 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** | **No. with given phenotype** | **Platelet reactivity measurement for the phenotype group**  **[metric]** | **SD/SE (report value and metric)** | **Statistical method** | **Mean difference (state if other metric)** | **95% CI of mean difference (state if other metric)** | **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)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Fontana, 2008{Fontana, 2008 182 /id}  17681590  Switzerland  NR | 600 mg clopidogrel loading dose; 75 mg maintenance dose; all patient except one were on aspirin at baseline; data NR for aspirin maintenance | CYP2C19 \*2 | PRI VASP continuous outcome | Measurement of PRI | After a minimum 15 d of clopidogrel treatment | \*2/\*2 | 2 | Mean = 66.1 | SD = 5.6 | Non-parametric tests for comparison of medians | NR | NR | 0.65 (across all 3 groups)  [Kruskall-Wallis test] | NO | NO | NO |
|  |  |  |  |  |  | \*2/\*1 | 25 | Mean = 50.6 | SD = 17.1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 54 | Mean = 50.9 | SD = 13.7 |  |  |  |  |  |  |  |
| Giusti, 2007{Giusti, 2007 190 /id}  18004210  Italy  NR | Loading dose: clopidogrel 600 mg (orally) + 500 mg ASA (IV); maintenance dose: clopidogrel 75 mg and ASA 100 mg (both daily) | CYP2C19 \*2 | Aggregation with ADP 2 μmol/L | % maximal aggregation (continuous) | 24 h after PCI (6 d for patients receiving IIb/IIIa inhibitors) | \*2/\*2 | 40 | 41  [median] | 5, 84  [range] | Non-parametric comparison of medians | NR | NR | P < 0.0001  (across 3 groups)  [Kruskall-Wallis]  P < 0.0001  (\*2/\*1 vs. \*1/\*1)  [Mann-Whitney]  P < 0.0001  (\*2/\*2 vs. \*1/\*1)  [Mann-Whitney]  P = 0.028  (\*2/\*2 vs. \*2/\*1)  [Mann-Whitney] | NO | NO | None. |
|  |  |  |  |  |  | \*2/\*1 | 405 | 32  [median] | 1, 94  [range] |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 974 | 26  [median] | 1,100  [range] |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/2 or \*2/\*1  (carriers) | 445 | 33  [median] | 1, 94  [range] | Non-parametric comparison of medians | NR | NR | P < 0.0001  (carriers vs. non-carriers)  [Mann-Whitney] | NO | NO | None. |
|  |  |  |  |  |  | \*1/\*1 (non-carriers) | 974 | 26  [median] | 1, 100  [range] |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 | 40 | 62  [median] | 26, 100  [range] | Non-parametric comparison of medians | NR | NR | P < 0.0001  (across 3 groups)  [Kruskall-Wallis]  P < 0.0001  (\*2/\*1 vs. \*1/\*1)  [Mann-Whitney]  P < 0.0001  (\*2/\*2 vs. \*1/\*1)  [Mann-Whitney]  P = 0.015  (\*2/\*2 vs. \*2/\*1)  [Mann-Whitney] | NO | NO | None. |
|  |  |  |  |  |  | \*2/\*1 | 405 | 54  [median] | 2, 100  [range] |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 974 | 49  [median] | 1, 100  [range] |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/2 or \*2/\*1  (carriers) | 445 | 56  [median] | 2, 100  [range] | Non-parametric comparison of medians | NR | NR | P < 0.0001  (carriers vs. non-carriers)  [Mann-Whitney] | NO | NO | None. |
|  |  |  |  |  |  | \*1/\*1 (non-carriers) | 974 | 49  [median] | 1, 100  [range] |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/2 or \*2/\*1  (carriers) | 445 | NR | NR | Linear regression | Coefficient = 5.3  Coefficient = 4.9 | SE = 1.0  SE = 1.3 | P < 0.0001  (carriers vs. non-carriers)  [univariable linear regression]  P = 0.0001  (carriers vs. non-carriers)  [linear regression] | NO  YES (age, sex, HTN, diabetes mellitus, dyslipidemia, smoking habits) | NO | None. |
|  |  |  |  |  |  | \*1/\*1 (non-carriers) | 974 | NR | NR |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/2 or \*2/\*1  (carriers) | 445 | NR | NR | Linear regression | Coefficient = 5.8  Coefficient = 5.5 | SE = 1.2  SE = 1.3 | P < 0.0001  (carriers vs. non-carriers)  [univariable linear regression]  P = 0.0001  (carriers vs. non-carriers)  [linear regression] | NO  YES (age, sex, HTN, diabetes mellitus, dyslipidemia, smoking habits) | NO | None. |
|  |  |  |  |  |  | \*1/\*1 (non-carriers) | 974 | NR | NR |  |  |  |  |  |  |  |
| Giusti, 2009{Giusti, 2009 134 /id}  19268736  Italy  RECLOSE 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). | CYP2C19\*2 | ADP-RPR | Continuous measurement | 12-18 h from clopidogrel loading | \*2/\*2 or \*2/\*1 | N = 247 | 51% [median] | 2%-100% [range] | Mann-Whitney U test | NR | NR | 0.001 | NO | NO | None |
|  |  |  |  |  |  | \*1/\*1 | N = 525 | 45% [median] | 1%-100% [range] |  |  |  |  |  |  |  |
| Gladding, 2009{Gladding, 2009 248 /id}  19926050  New Zealand  NR | Clopidogrel 150 mg daily | Autogenomics 2C19+ assay | Platelet inhibition (%) | Per VerifyNow | Baseline | CYP2C19\*2 carrier | NR | Median (range) 18% (0% to 72%) | NR | NR | NR | NR | 0.01 (vs. next row)  [Wilcoxon] | NO | NO | NONE |
|  |  |  |  |  |  | CYP2C19\*1/\*1 | NR | Median (range) 59% (11% to 95%) | NR |  |  |  |  |  |  |  |
|  |  |  |  |  | 7 days | CYP2C19\*2 carrier | NR | NR | NR | NR | NR | NR | 0.03 (vs. next row)  [Wilcoxon] | NR | NR | NONE |
|  |  |  |  |  |  | CYP2C19\*1/\*1 | NR | NR | NR |  |  |  |  |  |  |  |
|  |  |  | Change in platelet inhibition (%) from baseline |  | 7 days | CYP2C19\*2 carrier | NR | Mean (SD) 9% (11%) | NR | NR | NR | NR | 0.03 for this row’s result (7 days vs. baseline) [Student’s t] | NR | NR | Fig. 3 shows all raw data for this row and a P of 0.05 (?) |
|  |  |  |  |  |  | CYP2C19\*2 and CYP2C9\*3) carriers: poor or intermediate metabolizers | NR | Mean -10%  95% CI -20 to -0.1% | NR | NR | NR | NR | 0.05 (vs. wild type)  [Student’s t] | NO | NO | Raw data (separate for poor and intermediate, though result here is combined?) in Fig 4 |
| Jinnai, 2009{Jinnai, 2009 120 /id}  19531897  Japan  Partly industry funded | Patients were on low-dose aspirin (81-100 mg/day) at study enrollment. They received clopidogrel 300 mg loading dose on the first day and 75 mg daily maintenance thereafter. | CYP2C19 \*2, \*3 and \*1 | IPA | Change in platelet reactivity compared to baseline | 48h | PM = \*2/\*2 or \*2/\*3 | N = 6 | 16.0  [Mean % IPA] | SD = 13.0 | T-test | NR | NR | 0.04  (IM vs. EM) | NO | NO | Patient level data in figure 2b; data for other time-points in Figure 3 (individual patient data) |
|  |  |  |  |  |  | IM = \*2/\*1 or \*3/\*1 | N = 8 | 18.4  [Mean % IPA] | SD = 10.0 | T-test | NR | NR | 0.02  (PM vs. EM) | NO | NO |  |
|  |  |  |  |  |  | EM = \*1/\*1 | N = 11 | 31.6  [Mean % IPA] | SD = 14.3 | T-test | NR | NR | 0.73 (PM vs. IM) | NO | NO |  |
| Shuldiner, 2009{Shuldiner, 2009 116 /id}  19706858  USA  Sinai Hospital of Baltimore Study | Clopidogrel LD= 600 mg (n=112) or 300 mg (n=25); No LD for subjects on clopidogrel maintenance therapy (n=90).  Aspirin: 81-325 mg aspirin daily for ≥1 week prior to PCI and 325 mg on the day of PCI. Post-PCI: Aspirin 325 mg/day and clopidogrel 75mg/day | CYP2C19 \*2 | Mean ADP-induced reactivity | Measurements of platelet reactivity before and after clopidogrel administration | Pre-clopidogrel vs. post clopidogrel | \*2/\*2  \*2/\*1  \*1/\*1 | Pre clopidogrel N per group was \*2/\*2 = 4; \*2/\*1 = 37; \*1/\*1 = 102  (total=143)  Post-clopidogrel N per group was \*2/\*2 = 3; \*2/\*1 = 54; \*1/\*1 = 131  (total=188) | Means can only be extracted from Figure 3. | NR | Additive genetic model within each treatment period (pre-clopidogrel and post-clopidogrel); no comparisons of the genetic effect across treatment periods | NR | NR | P=0.92 for the difference between the 3 genotypes (additive model) pre-clopidogrel.  P=0.02 for the difference between the 3 genotypes (additive model) post-clopidogrel. | NO | NO | Measures were paired for some participants but data are not adequate to reconstruct before-after measurements. Patients receiving clopidogrel at baseline were excluded from baseline means. |
| Sibbing, 2010{Sibbing, 2010 95 /id}  20083681  Germany  Part of a prospective study of the Multiplate analyzer | Clopidogrel 600 mg loading dose; clopidogrel 75 mg (1/d) and aspirin 100 mg (2/d) maintenance. | CYP2C19 \*17 | Platelet aggregation | Continuous outcome, Multiplate analyzer | All patients received a clopidogrel loading dose with a recommended pre-treatment interval of 2h; blood was sampled directly before PCI.  The median clopidogrel loading interval was 3.5h for \*1/\*1; 3.5 h for \*17/\*1; and 5.3 h for \*17/\*17. | \*17/\*17 | N = 76 | 189  [median, in arbitrary units \* minutes] | IQR = 119, 301 | Comparison of medians using non-parametric tests | NR | NR | P = 0.007 (across all groups)  P = 0.039 (\*17/\*1 vs \*1/\*1)  P = 0.008 (\*17/\*17 vs. \*1/\*1) | NO | NO | Additional data in Figure (medians and bootstrap-based 95% CIs) |
|  |  |  |  |  |  | \*17/\*1 | N = 546 | 215  [median, in arbitrary units \* minutes] | IQR = 140, 342 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | N = 902 | 238  [median, in arbitrary units \* minutes] | IQR = 146, 388 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*17/\*17 or \*17/\*1 | N = 622 | 213  [median, in arbitrary units \* minutes] | IQR = 136, 329 | Linear regression | Coefficient values (adjusted mean difference) = -32.3 | SE = 9.5 | P = 0.0006  (carriers vs. non-carriers) [multivariable linear regression]  P = 0.009 (non-parametric test, Wilcoxon) | YES  (age, sex, BMI, serum creatinine, use of PPIs, clopidogrel loading interval) | NO | None |
|  |  |  |  |  |  | \*1/\*1 | N = 902 | 238  [median, in arbitrary units \* minutes] | IQR = 146, 388 |  |  |  |  |  |  |  |
| Varenhorst, 2009{Varenhorst, 2009 122 /id}  19429918  Sweden  Genetic sub-study | Clopidogrel 600 mg loading dose; 75 mg maintenance | CYP2C19 genotyping | VASP phosphorylation measurements at multiple timepoints (continuous) | VASP PRI assay with flow cytometry | Samples were collected at baseline, 2 h and 24 h post-loading dose; also at day 14 ±3 and day 29 ±3, both before that day’s maintenance dose | Extensive metabolizers = \*17/\*17, \*1A/\*17, \*1A/\*1A | N = 37 | Only reported in graph [VASP PRI, means from a linear model] | Only reported in graph | Linear model with covariate for EM vs. RM | Only reported in graph | Only reported in graph | P<0.05 comparing EM vs. RM in the clopidogrel arm at 24 h, 14 d and 29 d | Yes  [the linear model include body weight as a covariate] | NO  (some attempt was made to limit multiple testing) | Figures 2 and 3 |
|  |  |  |  |  |  | Reduced metabolizers = \*1A/\*2A, \*1A/\*8, \*2A/\*2A | N = 9 | Only reported in graph [VASP PRI, means from a linear model] | Only reported in graph |  | Only reported in graph | Only reported in graph |  |  |  | Figures 2 and 3 |
| Frere, 2008{Frere, 2008 176 /id}  18394438  France  NONE | 600 mg loading dose of clopidogrel + 250 mg aspirin | CYP2C19 \*2 genotyping | VASP phosphorylation assay | Measurement of VASP phosphorylation | At the catheterization laboratory (≥12h after the loading dose) | CYP2C19 \*2/\*2  (rs4244285) | NR for this assay (455 patients received this assay) | 69.1 [mean of %PRI VASP] | SEM = 5.7 | General linear model with genotype as the explanatory variable | NR | NR | 0.0001 [across 3 groups]  0.0001  [across 3 groups]  <0.007  [recessive general linear  model]  <0.0001 [codominant general linear model across groups] | Unadjusted  Adjusted [age, sex]  Unadjusted  Unadjusted | NO | Additional data in Figure 1 (however reported statistics are adequate) |
|  |  |  |  |  |  | CYP2C19 \*2/\*1  (rs4244285) | NR for this assay (455 patients received this assay) | 59.1 [mean of %PRI VASP] | SEM = 2.1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19 \*1/\*1  (rs4244285) | NR for this assay (455 patients received this assay) | 50.9 [mean of %PRI VASP] | SEM = 1.3 |  |  |  |  |  |  |  |
|  | 600 mg loading dose of clopidogrel + 250 mg aspirin | CYP2C19 \*2 genotyping | ADP-induced aggregation by LTA | Measurement of ADP-stimulated aggregation | At the catheterization laboratory (≥12h after the loading dose) | CYP2C19 \*2/\*2  (rs4244285) | 23 | 66.1 [% change in light transmittance from baseline] | SEM = 4 | General linear model with genotype as the explanatory variable | NR | NR | 0.039 [across 3 groups]  0.05  [across 3 groups]  <0.01  [recessive general linear  model]  <0.08 [codominant general linear model across groups] | Unadjusted  Adjusted [age, sex]  Unadjusted  Unadjusted | NO | Additional data in Figure 1 (however reported statistics are adequate) |
|  |  |  |  |  |  | CYP2C19 \*2/\*1  (rs4244285) | 143 | 56.1 [% change in light transmittance from baseline] | SEM = 1.6 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19 \*1/\*1  (rs4244285) | 435 | 55.7 [% change in light transmittance from baseline] | SEM = 0.9 |  |  |  |  |  |  |  |
|  | 600 mg loading dose of clopidogrel + 250 mg aspirin | CYP2C19 \*2 genotyping | ADP-induced P-selectin expression | Measurement of P-selecting expression | At the catheterization laboratory (≥12h after the loading dose) | CYP2C19 \*2/\*2  (rs4244285) | NR for this assay (455 patients received this assay) | 0.43 [arbitrary units of fluorescence] | SEM = 0.04 | General linear model with genotype as the explanatory variable | NR | NR | 0.035 [across 3 groups]  0.030  [across 3 groups]  <0.06  [recessive general linear  model]  <0.009 [codominant general linear model across groups] | Unadjusted  Adjusted [age, sex]  Unadjusted  Unadjusted | NO | Additional data in Figure 1 (however reported statistics are adequate) |
|  |  |  |  |  |  | CYP2C19 \*2/\*1  (rs4244285) | NR for this assay (455 patients received this assay) | 0.39 [arbitrary units of fluorescence] | SEM = 0.01 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19 \*1/\*1  (rs4244285) | NR for this assay (455 patients received this assay) | 0.35 [arbitrary units of fluorescence] | SEM = 0.01 |  |  |  |  |  |  |  |
| Frere, 2009{Frere, 2009 117 /id}  19496924  France  Part of larger observational study | 600 mg clopidogrel loading dose | CYP2C19 \*4 | Both VASP and ADP-induced aggregation | Measurement of PRI-VASP and ADP-induced aggregation | After clopidogrel loading dose (exact timing NR) | NR | \*4/\*4=0  \*4/\*1=8  \*1/\*1=589 | NR | NR | Recessive and co-dominant models; analysis method NR | NR | NR | Non-significant | NR | NO | Only a text comment saying that these polymorphisms did not impact the reactivity measures |
|  |  | CYP2C19 \*5 | Both VASP and ADP-induced aggregation | Measurement of PRI-VASP and ADP-induced aggregation | After clopidogrel loading dose (exact timing NR) | NR | \*5/\*5=0  \*5/\*1=8  \*1/\*1=589 | NR | NR | Recessive and co-dominant models; analysis method NR | NR | NR | Non-significant | NR | NO | Only a text comment saying that these polymorphisms did not impact the reactivity measures |
|  |  | CYP2C19 \*6 | Both VASP and ADP-induced aggregation | Measurement of PRI-VASP and ADP-induced aggregation | After clopidogrel loading dose (exact timing NR) | NR | \*6/\*6=0  \*6/\*1=8  \*1/\*1=589 | NR | NR | Recessive and co-dominant models; analysis method NR | NR | NR | Non-significant | NR | NO | Only a text comment saying that these polymorphisms did not impact the reactivity measures |
|  |  | CYP2C19 \*17 | VASP phosphorylation assay | Measurement of PRI-VASP | After clopidogrel loading dose (exact timing NR) | \*17/\*17 | 25 | 45.79 [mean of % PRI VASP] | SD=17.71 | NR | NR | NR | 0.0206  [“chi square”] | NO | NO | P=0.19 for the interaction with CYP2C19 \*2 [analysis method NR] |
|  |  |  |  |  |  | \*17/\*1 | 189 | 50.11 [mean of % PRI VASP] | SD=24.3 |  |  |  |  |  | NO |  |
|  |  |  |  |  |  | \*1/\*1 | 382 | 55.9  [mean of % PRI VASP] | SD=22.80 |  |  |  |  |  | NO |  |
|  |  | CYP2C19 \*17 | VASP phosphorylation assay | Measurement of PRI-VASP | After clopidogrel loading dose (exact timing NR) | \*17/\*17 and \*17/\*1  (carriers vs. non-carriers) | 214 | 49.72  [mean of % PRI VASP] | SD=23.80 | NR |  | NR | 0.0073  [“chi-square”]  0.0005  [“chi square”] | NO | NO | P=0.08 for the interaction with CYP2C19 \*2 [analysis method NR] |
|  |  |  |  |  |  | \*1/\*1 | 382 | 55.9  [mean of % PRI VASP] | SD=22.80 |  |  |  |  |  | NO |  |
|  |  | CYP2C19 \*17 | ADP-induced aggregation (assay NR) | Measurement of ADP-induced aggregation | After clopidogrel loading dose (exact timing NR) | \*17/\*17 | 25 | 50.8  [Mean of % aggregation] | SD=27.30 | NR | NR | NR | 0.2813  [“chi square”] | NO | NO | None |
|  |  |  |  |  |  | \*17/\*1 | 189 | 55.5  [Mean of % aggregation] | SD=19.00 |  |  |  |  |  | NO |  |
|  |  |  |  |  |  | \*1/\*1 | 382 | 57.03  [Mean of % aggregation] | SD=18.50 |  |  |  |  |  | NO |  |
|  |  | CYP2C19 \*17 | ADP-induced aggregation (assay NR) | Measurement of ADP-induced aggregation | After clopidogrel loading dose (exact timing NR) | \*17/\*17 and \*17/\*1  (carriers vs. non-carriers) | 214 | 54.96  [Mean of % aggregation] | SD=20.10 | NR | NR | NR | 0.2062  [“chi square”] | NO | NO | None |
|  |  |  |  |  |  | \*1/\*1 | 382 | 57.03  [Mean of % aggregation] | SD=18.50 |  |  |  |  |  | NO |  |
| Harmsze 2010{Harmsze, 2010 102 /id}  19934793  Netherlands  NR | clopidogrel maintenance 75 mg/day | CYP2C19\*2 | On-clopidogrel platelet reactivity | Maximal platelet aggregation  achieved in any time during the run of 10 min with ADP 5 μmol/L | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 6.7 | 3.6,9.8 | P<0.001 [Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)] | NO | NR |  |
|  |  |  |  |  |  | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 6.9 | 3.7,10 | 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. |  |  |
|  |  |  | On-clopidogrel platelet reactivity | Maximal platelet aggregation  achieved in any time during the run of 10 min with ADP 20 μmol/L | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 6.3 | 3.4,9.3 | P<0.001 [Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)] | NO | NR |  |
|  |  |  |  |  |  |  |  |  |  | Linear regression | 7 | 4,10 | 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. |  |  |
|  |  |  | On-clopidogrel platelet reactivity | on-clopidogrel platelet reactivity expressed as P2Y12 reaction units (PRU) | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 35.1 | 17.2,53 | P<0.001 [Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)] | NO | NR |  |
|  |  |  |  |  |  |  |  |  |  | Linear regression | 34.8 | 16.8,52.8 | 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. |  |  |
| Harmsze 2010{Harmsze, 2010 102 /id}  19934793  Netherlands | 300 mg clopidogrel loading dose | CYP2C19\*2 | On-clopidogrel platelet reactivity | Maximal platelet aggregation  achieved in any time during the run of 10 min with ADP 5 μmol/L | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 7.8 | 3.9,12.6 | P=0.002 [Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)] | NO | NR |  |
|  |  |  |  |  |  | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 5.7 | 0.6,10.8 | P=0.028 [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. |  |  |
|  |  |  | On-clopidogrel platelet reactivity | Maximal platelet aggregation  achieved in any time during the run of 10 min with ADP 20 μmol/L | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 7.4 | 3.3,11.6 | P=0.001 [Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)] | NO | NR |  |
|  |  |  |  |  |  |  |  |  |  | Linear regression | 7 | 2.6,11.5 | P=0.002 [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. |  |  |
|  |  |  | On-clopidogrel platelet reactivity | on-clopidogrel platelet reactivity expressed as P2Y12 reaction units (PRU) | NR (Before stenting) | Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1) | NR | NR | NR | Linear regression | 37.5 | 16.5,58.5 | P=0.001 [Carriers (\*1/\*2 or \*2/\*2) vs Noncarriers (\*1/\*1)] | NO | NR |  |
|  |  |  |  |  |  |  |  |  |  | Linear regression | 28.5 | 7.1,549.6 | P=0.009 [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. |  |  |
| Tantry 2010{Tantry, 2010 39 /id}  21079055  Multicountry - North America and Europe  Genetic substtudy of ONSET/OFFSET and RESPOND | All patients received 75 to 100 mg/d aspirin clopidogrel (600-mg load, 75 mg/d thereafter) | TaqMan | 5 uM ADP-induced platelet aggregation (%) | NR | 8 hr after loading dose | UM | 28 | see fig 3A | see fig 3A | Kruskal-Wallis (K-W) test | NR | NR | 0.289 for this and next 3 rows [K-W] | NO | NO | Get data from Fig. 3A |
|  |  |  |  |  |  | EM | 31 | see fig 3A | see fig 3A |  |  |  |  |  |  | Get data from Fig. 3A |
|  |  |  |  |  |  | IM | 20 | see fig 3A | see fig 3A |  |  |  |  |  |  | Get data from Fig. 3A |
|  |  |  |  |  |  | PM | 3 | see fig 3A | see fig 3A |  |  |  |  |  |  | Get data from Fig. 3A |
|  |  |  |  |  | 8 hr after last maintenance dose | UM | 28 | see fig 3B | see fig 3B |  |  |  | 0.33 for this and next 3 rows [K-W] |  |  | Get data from Fig. 3B |
|  |  |  |  |  |  | EM | 31 | see fig 3B | see fig 3B |  |  |  |  |  |  | Get data from Fig. 3B |
|  |  |  |  |  |  | IM | 20 | see fig 3B | see fig 3B |  |  |  |  |  |  | Get data from Fig. 3B |
|  |  |  |  |  |  | PM | 3 | see fig 3B | see fig 3B |  |  |  |  |  |  | Get data from Fig. 3B |
|  |  |  | 20 uM ADP-induced platelet aggregation (%) |  | 8 hr after loading dose | UM | 28 | see fig 4A | see fig 4A |  |  |  | 0.307 for this and next 3 rows [K-W] |  |  | Get data from Fig. 4A |
|  |  |  |  |  |  | EM | 31 | see fig 4A | see fig 4A |  |  |  |  |  |  | Get data from Fig. 4A |
|  |  |  |  |  |  | IM | 20 | see fig 4A | see fig 4A |  |  |  |  |  |  | Get data from Fig. 4A |
|  |  |  |  |  |  | PM | 3 | see fig 4A | see fig 4A |  |  |  |  |  |  | Get data from Fig. 4A |
|  |  |  |  |  | 8 hr after last maintenance dose | UM | 28 | see fig 4B | see fig 4B |  |  |  | 0.056 for this and next 3 rows [K-W] |  |  | Get data from Fig. 4B |
|  |  |  |  |  |  | EM | 31 | see fig 4B | see fig 4B |  |  |  |  |  |  | Get data from Fig. 4B |
|  |  |  |  |  |  | IM | 20 | see fig 4B | see fig 4B |  |  |  |  |  |  | Get data from Fig. 4B |
|  |  |  |  |  |  | PM | 3 | see fig 4B | see fig 4B |  |  |  |  |  |  | Get data from Fig. 4B |
|  |  |  | VerifyNow P2Y12 reaction units |  | 8 hr after loading dose | UM | 28 | see fig 5A | see fig 5A |  |  |  | 0.019 for this and next 3 rows [K-W] |  |  | Get data from Fig. 5A |
|  |  |  |  |  |  | EM | 31 | see fig 5A | see fig 5A |  |  |  |  |  |  | Get data from Fig. 5A |
|  |  |  |  |  |  | IM | 20 | see fig 5A | see fig 5A |  |  |  |  |  |  | Get data from Fig. 5A |
|  |  |  |  |  |  | PM | 3 | see fig 5A | see fig 5A |  |  |  |  |  |  | Get data from Fig. 5A |
|  |  |  |  |  | 8 hr after last maintenance dose | UM | 28 | see fig 5B | see fig 5B |  |  |  | 0.006 for this and next 3 rows [K-W] |  |  | Get data from Fig. 5B |
|  |  |  |  |  |  | EM | 31 | see fig 5B | see fig 5B |  |  |  |  |  |  | Get data from Fig. 5B |
|  |  |  |  |  |  | IM | 20 | see fig 5B | see fig 5B |  |  |  |  |  |  | Get data from Fig. 5B |
|  |  |  |  |  |  | PM | 3 | see fig 5B | see fig 5B |  |  |  |  |  |  | Get data from Fig. 5B |
|  |  |  | VASP platelet reactiveity index (%) |  | 8 hr after loading dose | UM | 28 | see fig 6A | see fig 6A |  |  |  | 0.153 for this and next 3 rows [K-W] |  |  | Get data from Fig. 6A |
|  |  |  |  |  |  | EM | 31 | see fig 6A | see fig 6A |  |  |  |  |  |  | Get data from Fig. 6A |
|  |  |  |  |  |  | IM | 20 | see fig 6A | see fig 6A |  |  |  |  |  |  | Get data from Fig. 6A |
|  |  |  |  |  |  | PM | 3 | see fig 6A | see fig 6A |  |  |  |  |  |  | Get data from Fig. 6A |
|  |  |  |  |  | 8 hr after last maintenance dose | UM | 28 | see fig 6B | see fig 6B |  |  |  | 0.069 for this and next 3 rows [K-W] |  |  | Get data from Fig. 6B |
|  |  |  |  |  |  | EM | 31 | see fig 6B | see fig 6B |  |  |  |  |  |  | Get data from Fig. 6B |
|  |  |  |  |  |  | IM | 20 | see fig 6B | see fig 6B |  |  |  |  |  |  | Get data from Fig. 6B |
|  |  |  |  |  |  | PM | 3 | see fig 6B | see fig 6B |  |  |  |  |  |  | Get data from Fig. 6B |
|  |  |  | 5 mM ADP-induced platelet aggregation (%) |  | 8 hr after loading dose | LOF allele carrier | 23 | see fig 3A | see fig 3A |  |  |  | 0.078 vs. next row [K-W] |  |  | Get data from Fig. 3A |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 3A | see fig 3A |  |  |  |  |  |  | Get data from Fig. 3A |
|  |  |  |  |  | 8 hr after last maintenance dose | LOF allele carrier | 23 | see fig 3B | see fig 3B |  |  |  | 0.097vs. next row [K-W] |  |  | Get data from Fig. 3B |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 3B | see fig 3B |  |  |  |  |  |  | Get data from Fig. 3B |
|  |  |  | 20 mM ADP-induced platelet aggregation (%) |  | 8 hr after loading dose | LOF allele carrier | 23 | see fig 4A | see fig 4A |  |  |  | 0.080 vs. next row [K-W] |  |  | Get data from Fig. 4A |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 4A | see fig 4A |  |  |  |  |  |  | Get data from Fig. 4A |
|  |  |  |  |  | 8 hr after last maintenance dose | LOF allele carrier | 23 | see fig 4B | see fig 4B |  |  |  | 0.049vs. next row [K-W] |  |  | Get data from Fig. 4B |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 4B | see fig 4B |  |  |  |  |  |  | Get data from Fig. 4B |
|  |  |  | VerifyNow P2Y12 reaction units |  | 8 hr after loading dose | LOF allele carrier | 23 | see fig 5A | see fig 5A |  |  |  | 0.010 vs. next row [K-W] |  |  | Get data from Fig. 5A |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 5A | see fig 5A |  |  |  |  |  |  | Get data from Fig. 5A |
|  |  |  |  |  | 8 hr after last maintenance dose | LOF allele carrier | 23 | see fig 5B | see fig 5B |  |  |  | 0.002 vs. next row [K-W] |  |  | Get data from Fig. 5B |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 5B | see fig 5B |  |  |  |  |  |  | Get data from Fig. 5B |
|  |  |  | VASP platelet reactiveity index (%) |  | 8 hr after loading dose | LOF allele carrier | 23 | see fig 6A | see fig 6A |  |  |  | 0.036 vs. next row [K-W] |  |  | Get data from Fig. 6A |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 6A | see fig 6A |  |  |  |  |  |  | Get data from Fig. 6A |
|  |  |  |  |  | 8 hr after last maintenance dose | LOF allele carrier | 23 | see fig 6B | see fig 6B |  |  |  | 0.010 vs. next row [K-W] |  |  | Get data from Fig. 6B |
|  |  |  |  |  |  | LOF allele noncarrier | 59 | see fig 6B | see fig 6B |  |  |  |  |  |  | Get data from Fig. 6B |
|  |  |  | 5 uM ADP-induced platelet aggregation (%) |  | 8 hr after loading dose | GOF allele carrier | 28 | see fig 3A | see fig 3A |  |  |  | 0.0168 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 3A |
|  |  |  |  |  | 8 hr after last maintenance dose | GOF allele carrier | 28 | see fig 3B | see fig 3B |  |  |  | 0.231 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 3B |
|  |  |  | 20 uM ADP-induced platelet aggregation (%) |  | 8 hr after loading dose | GOF allele carrier | 28 | see fig 4A | see fig 4A |  |  |  | 0.165 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 4A |
|  |  |  |  |  | 8 hr after last maintenance dose | GOF allele carrier | 28 | see fig 4B | see fig 4B |  |  |  | 0.080 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 4B |
|  |  |  | VerifyNow P2Y12 reaction units |  | 8 hr after loading dose | GOF allele carrier | 28 | see fig 5A | see fig 5A |  |  |  | 0.028 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 5A |
|  |  |  |  |  | 8 hr after last maintenance dose | GOF allele carrier | 28 | see fig 5B | see fig 5B |  |  |  | 0.007 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 5B |
|  |  |  | VASP platelet reactiveity index (%) |  | 8 hr after loading dose | GOF allele carrier | 28 | see fig 6A | see fig 6A |  |  |  | 0.109 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 6A |
|  |  |  |  |  | 8 hr after last maintenance dose | GOF allele carrier | 28 | see fig 6B | see fig 6B |  |  |  | 0.034 for this row and correspondign LOF carrier and EM above [K-W] |  |  | Get data from Fig. 6B |
|  |  |  | 5 uM ADP-induced platelet aggregation (%) |  | 8 hr after last maintenance dose | \*1/\*1 | 31 | see fig 7A | see fig 7A |  |  |  | NR |  |  | Get data from Fig. 7A |
|  |  |  |  |  |  | \*1/\*2 | 13 | see fig 7A | see fig 7A |  |  |  |  |  |  | Get data from Fig. 7A |
|  |  |  |  |  |  | \*1/\*3 | 1 | see fig 7A | see fig 7A |  |  |  |  |  |  | Get data from Fig. 7A |
|  |  |  |  |  |  | \*1/\*17 | 28 | see fig 7A | see fig 7A |  |  |  |  |  |  | Get data from Fig. 7A |
|  |  |  |  |  |  | \*2/\*2 | 3 | see fig 7A | see fig 7A |  |  |  |  |  |  | Get data from Fig. 7A |
|  |  |  |  |  |  | \*2/\*17 | 6 | see fig 7A | see fig 7A |  |  |  |  |  |  | Get data from Fig. 7A |
|  |  |  | 20 uM ADP-induced platelet aggregation (%) |  | 8 hr after last maintenance dose | \*1/\*1 | 31 | see fig 7B | see fig 7B |  |  |  |  |  |  | Get data from Fig. 7B |
|  |  |  |  |  |  | \*1/\*2 | 13 | see fig 7B | see fig 7B |  |  |  |  |  |  | Get data from Fig. 7B |
|  |  |  |  |  |  | \*1/\*3 | 1 | see fig 7B | see fig 7B |  |  |  |  |  |  | Get data from Fig. 7B |
|  |  |  |  |  |  | \*1/\*17 | 28 | see fig 7B | see fig 7B |  |  |  |  |  |  | Get data from Fig. 7B |
|  |  |  |  |  |  | \*2/\*2 | 3 | see fig 7B | see fig 7B |  |  |  |  |  |  | Get data from Fig. 7B |
|  |  |  |  |  |  | \*2/\*17 | 6 | see fig 7B | see fig 7B |  |  |  | 0.0995 for this and 5 previous rows [K-W] |  |  | Get data from Fig. 7B |
|  |  |  | VerifyNow P2Y12 reaction units |  | 8 hr after last maintenance dose | \*1/\*1 | 31 | see fig 7C | see fig 7C |  |  |  |  |  |  | Get data from Fig. 7C |
|  |  |  |  |  |  | \*1/\*2 | 13 | see fig 7C | see fig 7C |  |  |  |  |  |  | Get data from Fig. 7C |
|  |  |  |  |  |  | \*1/\*3 | 1 | see fig 7C | see fig 7C |  |  |  |  |  |  | Get data from Fig. 7C |
|  |  |  |  |  |  | \*1/\*17 | 28 | see fig 7C | see fig 7C |  |  |  |  |  |  | Get data from Fig. 7C |
|  |  |  |  |  |  | \*2/\*2 | 3 | see fig 7C | see fig 7C |  |  |  |  |  |  | Get data from Fig. 7C |
|  |  |  |  |  |  | \*2/\*17 | 6 | see fig 7C | see fig 7C |  |  |  | ≤0.006 for this and 5 previous rows [K-W] |  |  | Get data from Fig. 7C |
|  |  |  | VASP platelet reactiveity index (%) |  | 8 hr after last maintenance dose | \*1/\*1 | 31 | see fig 7D | see fig 7D |  |  |  |  |  |  | Get data from Fig. 7D |
|  |  |  |  |  |  | \*1/\*2 | 13 | see fig 7D | see fig 7D |  |  |  |  |  |  | Get data from Fig. 7D |
|  |  |  |  |  |  | \*1/\*3 | 1 | see fig 7D | see fig 7D |  |  |  |  |  |  | Get data from Fig. 7D |
|  |  |  |  |  |  | \*1/\*17 | 28 | see fig 7D | see fig 7D |  |  |  |  |  |  | Get data from Fig. 7D |
|  |  |  |  |  |  | \*2/\*2 | 3 | see fig 7D | see fig 7D |  |  |  |  |  |  | Get data from Fig. 7D |
|  |  |  |  |  |  | \*2/\*17 | 6 | see fig 7D | see fig 7D |  |  |  | 0.0996 for this and 5 previous rows [K-W] |  |  | Get data from Fig. 7D |
| Jeong 2010{Jeong, 2010 70 /id}  20650435  Korea  NR | high-MD clopidogrel of 150 mg/day | CYP2C19 | Platelet reactivity (max) | LTA, 5uM ADP | 2-4 hours | \*1/\*1 | 46 | 30.3 | 12.6 | t-test | NR | NR | <0.001 comparing the following row | NR | NR |  |
|  |  |  |  |  |  | RMs |  | 40.7 | 16.8 |  |  |  |  |  |  |  |
|  |  |  | Platelet reactivity (late) | LTA, 5uM ADP | 2-4 hours | \*1/\*1 | 46 | 17.5 | 12.6 | t-test | NR | NR | 0.001 comparing the following row | NR | NR |  |
|  |  |  |  |  |  | RMs |  | 28.8 | 19.6 |  |  |  |  |  |  |  |
|  |  |  | Platelet reactivity (max) | LTA, 20uM ADP | 2-4 hours | \*1/\*1 | 46 | 40.5 | 15.8 | t-test | NR | NR | <0.001 comparing the following row | NR | NR |  |
|  |  |  |  |  |  | RMs |  | 54.2 | 16.2 |  |  |  |  |  |  |  |
|  |  |  | Platelet reactivity (late) | LTA, 20uM ADP | 2-4 hours | \*1/\*1 | 46 | 24.3 | 17.7 | t-test | NR | NR | 0.001 comparing the following row | NR | NR |  |
|  |  |  |  |  |  | RMs |  | 42 | 21.7 |  |  |  |  |  |  |  |
|  |  |  | VerifyNow P2Y12 assay(PRU) | ADP | 2-4 hours | \*1/\*1 | 46 | 149.3 | 74.5 | t-test | NR | NR | 0.001 comparing the following row | NR | NR |  |
|  |  |  |  |  |  | RMs |  | 197.7 | 78.1 |  |  |  |  |  |  |  |
|  |  |  | VerifyNow P2Y12 assay(PRU), % inhibition | ADP | 2-4 hours | \*1/\*1 | 46 | 55.7 | 20.4 | t-test | NR | NR | 0.001 comparing the following row | NR | NR |  |
|  |  |  |  |  |  | RMs |  | 37.6 | 22.4 |  |  |  |  |  |  |  |
| Barker, 2010{Barker, 2010 52 /id}  20965456  USA  NR | clopidogrel  150 mg/day for 7 days | CYP2C19 | OTR | P2Y12 reaction units (PRU) | after 7 days | Lof allele |  | 292 | 40 | t-test | NR | NR | 0.5 | no | no |  |
|  |  |  |  |  |  | Vs  Non-carriers |  | 281 | 54 |  |  |  |  |  |  |  |
|  | clopidogrel  150 mg/day for 7 days | CYP2C19 | OTR | P2Y12 reaction units (PRU) | after 7 days | Lof allele |  | 52 | 66 | t-test | NR | NR | 0.25 | no | no |  |
|  |  |  |  |  |  | Vs  Non-carriers |  | 77 | 72 |  | NR | NR |  |  |  |  |
|  |  |  | OTR | P2Y12 reaction units (PRU) | after 7 days | CYP2C19 |  | 61 | 75 | ANOVA | NR | NR | 0.5 | no | no |  |
|  |  |  | OTR | P2Y12 reaction units (PRU) | after 7 days | CYP2C19 |  | 84 | 72 |  | NR | NR |  |  |  |  |
|  |  |  | OTR | P2Y12 reaction units (PRU) | after 7 days | CYP2C19 |  | 56 | 71 |  | NR | NR |  |  |  |  |
|  |  |  | OTR | P2Y12 reaction units (PRU) | after 7 days | CYP2C19 |  | 28 | 31 |  | NR | NR |  |  |  |  |
| Bonello, 2010{Bonello, 2010 45 /id}  20708365  France  NR | All patients received oral LDs of 250 mg aspirin and 600 mg clopidogrel at least 6 h before the first VASP index measurement | CYP2C19 | VASP index | Median fluorescence intensity (MFI) | 12 h | Carrier of 1 mutant allele | 411 | 61.7 | 18.4% | t-test | NR | NR | <0.001 compared with the second row | NR | NR |  |
|  |  |  | VASP index | Median fluorescence intensity (MFI) | 12h | Wild-type allele homozygotes | 411 | 49.2 | 24.2% | t-test | NR | NR |  | NR | NR |  |
|  |  |  | VASP index | Median fluorescence intensity (MFI) | First dose | Carrier of at least one CYP2C19\*2 allele | 103 | 69.7 | 10.1% | t-test | NR | NR | <0.0001 compare with the lower row | NR | NR |  |
|  |  |  | VASP index | Median fluorescence intensity (MFI) | Second dose | Carrier of at least one CYP2C19\*2 allele | 103 | 50.6 | 17.6% | t-test | NR | NR |  | NR | NR |  |
| Hwang 2011{Hwang, 2011 35 /id}  21075428  South Korea  NR | 300-mg loading dose (LD) of clopidogrel and aspirin 200 mg/day maintenance dose of aspirin and 75 mg/day of clopidogrel thereafter. | CYP2C19\*2 | Platelet measures | 5 umol/L ADP-MPA,% | 12h | Codominant | GG 93 | 43.6 | 15.2 | ANOVA | NR | NR | 0.003 comparing with the following 2 groups | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | Codominant | GA  79 | 50.6 | 15.1 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | Codominant | AA  18 | 53.0 | 14.7 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | dominant | GG  93 | 43.6 | 15.2 | t- test | NR | NR | 0.001 comparing with the following group | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | dominant | GA/AA 97 | 51.1 | 14.9 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | recessive | GG/GA 172 | 46.8 | 15.5 | t- test | NR | NR | 0.107 comparing with the following group | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | recessive | AA  18 | 53 | 14.7 |  | NR | NR |  | NR | Yes |  |
|  |  | CYP2C19\*3 | Platelet measures | 5 umol/L ADP-MPA,% | 12h | Codominant | GG  165 | 46.3 | 15.5 | ANOVA | NR | NR | 0.008 comparing with the following 2 groups | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | Codominant | GA  25 | 55.1 | 13.7 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | Codominant | AA  0 | - | - |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | dominant | GG  165 | 46.3 | 15.5 | t- test | NR | NR | 0.008 comparing with the following group | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | dominant | GA/AA 25 | 55.1 | 13.7 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | recessive | GG/GA 190 | 47.4 | 15.5 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 5 umol/L ADP-MPA,% | 12h | recessive | AA  0 | - | - |  | NR | NR |  | NR | Yes |  |
|  |  | CYP2C19\*2 | Platelet measures | 20 umol/L ADP-MPA,% | 12h | Codominant | GG  93 | 56.7 | 15.4 | ANOVA | NR | NR | <0.001  comparing with the following 2 group | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | Codominant | GA  79 | 63.8 | 12 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | Codominant | AA  18 | 67.5 | 10.5 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | dominant | GG  93 | 56.7 | 15.4 | t- test | NR | NR | <0.001  comparing with the following group | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | dominant | GA/AA  97 | 64.5 | 11.8 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | recessive | GG/GA  172 | 59.9 | 14.3 | t- test | NR | NR | 0.03  comparing with the following group | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | recessive | AA  18 | 67.5 | 10.5 |  | NR | NR |  | NR | Yes |  |
|  |  | CYP2C19\*3 | Platelet measures | 20 umol/L ADP-MPA,% | 12h | Codominant | GG  165 | 59.7 | 14.4 | ANOVA | NR | NR | 0.008 comparing with the following 2 groups | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | Codominant | GA  25 | 67.2 | 10.3 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | Codominant | AA  0 | - | - |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | dominant | GG  165 | 59.7 | 14.4 | t- test | NR | NR | 0.008 comparing with the following group | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | dominant | GA/AA 25 | 67.2 | 10.3 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | recessive | GG/GA 190 | 60.7 | 14.2 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | 20 umol/L ADP-MPA,% | 12h | recessive | AA  0 | - | - |  | NR | NR |  | NR | Yes |  |
|  | Clopidogrel | CYP2C19\*2 | Platelet measures | P2Y12 reaction unit | 12h | Codominant | GG  93 | 256.5 | 77.7 | ANOVA | NR | NR | 0.081  Comparing with the following 2 groups | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | Codominant | GA  79 | 270.9 | 71.9 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | Codominant | AA  18 | 297.6 | 68.3 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | dominant | GG  93 | 256.5 | 77.7 | t- test | NR | NR | 0.075 Comparing with the following group | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | dominant | GA/AA  97 | 275.9 | 71.7 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | recessive | GG/GA  172 | 263.1 | 75.2 | t- test | NR | NR | 0.064  Comparing with the following group | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | recessive | AA  18 | 297.6 | 68.3 |  | NR | NR |  | NR | Yes |  |
|  |  | CYP2C19\*3 | Platelet measures | P2Y12 reaction unit | 12h | Codominant | GG  165 | 264 | 76.9 | ANOVA | NR | NR | 0.258 Comparing with the following 2 groups | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | Codominant | GA  25 | 282.2 | 60.5 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | Codominant | AA  0 | - | - |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | dominant | GG  165 | 264 | 76.9 | t- test | NR | NR | 0.258  Comparing with the following group | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | dominant | GA/AA 25 | 282.2 | 60.5 |  | NR | NR |  | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | recessive | GG/GA  190 | 266.4 | 75.1 |  | NR | NR | - | NR | Yes |  |
|  |  |  |  | P2Y12 reaction unit | 12h | recessive | AA  0 | - | - |  | NR | NR |  | NR | Yes |  |
| Kang, 2010{Kang, 2010 40 /id}  20724801  Korea  NR | 300-mg LD of clopidogrel and aspirin followed by 200 mg/day MD of aspirin and 75 mg/day clopidogrel | CYP2C19 | 5 umol/L ADP PRmax | Maximal platelet reactivity | NR | mutant allele | 104 | 51.6 | 16.4 | t-test | NR | NR | 0.008 (mutant allele  Vs no carrier) | NR | NR |  |
|  |  |  |  |  |  | No mutant carrier | 72 | 44.7 | 17.4 |  |  |  |  |  |  |  |
|  |  | CYP2C19 | 20 umol/L ADP  PRmax | Maximal platelet reactivity | NR | mutant allele | 104 | 64.6 | 13.9 | t-test | NR | NR | 0.007 | NR | NR |  |
|  |  |  |  |  |  | No mutant carrier | 72 | 58.2 | 17.4 |  |  |  |  |  |  |  |
| Liu 2010{Liu, 2010 38 /id}  21163112  China  NR | 300 mg clopidogrel and a daily maintenance dose of 75 mg | SNP rs4244285 | Platelet aggregation | maximal percent change in LTA from the baseline value | At baseline | G/G, | 426 | 62.8 | 6.6 | t-test | NR | NR | P=0.756 | NR | NR |  |
|  |  |  |  | maximal percent change in LTA from the baseline value | At baseline | G/A or A/A | 296 | 62.7 | 7.1 |  | NR | NR |  | NR | NR |  |
|  |  |  |  | maximal percent change in LTA from the baseline value | After loading | G/G, | 426 | 36.3 | 11.5 | t-test | NR | NR | P=0.039 | NR | NR |  |
|  |  |  |  | maximal percent change in LTA from the baseline value | After loading | G/A or A/A | 296 | 38.1 | 11.6 |  | NR | NR |  | NR | NR |  |
|  |  |  |  | maximal percent change in LTA from the baseline value | Reduction | G/G, | 426 | 26.9 | 12.3 | t-test | NR | NR | P=0.038 | NR | NR |  |
|  |  |  |  | maximal percent change in LTA from the baseline value | Reduction | G/A or A/A | 296 | 24.5 | 12.8 |  | NR | NR |  | NR | NR |  |
|  |  | Smoking | Platelet aggregation | maximal percent change in LTA from the baseline value | At baseline | smoking | 312 | 63.8±6.8 | 63.8±6.8 | t-test | NR | NR | P<0.001 | NR | NR |  |
|  |  | Non-smoking | Platelet aggregation | maximal percent change in LTA from the baseline value | At baseline | Non-smoking | 410 | 62.0±6.8 | 62.0±6.8 |  | NR | NR |  | NR | NR |  |
|  |  | Smoking | Platelet aggregation | maximal percent change in LTA from the baseline value | After loading | smoking | 312 | 36.0±12.3 | 36.0±12.3 | t-test | NR | NR | P=0.041 | NR | NR |  |
|  |  | Non-smoking | Platelet aggregation | maximal percent change in LTA from the baseline value | After loading | Non-smoking | 410 | 37.8±10.9 | 37.8±10.9 |  | NR | NR |  | NR | NR |  |
|  |  | Smoking | Platelet aggregation | maximal percent change in LTA from the baseline value | Reduction | smoking | 312 | 27.8±13.2 | 27.8±13.2 | t-test | NR | NR | P<0.001 | NR | NR |  |
|  |  | Non-smoking | Platelet aggregation | maximal percent change in LTA from the baseline value | Reduction | Non-smoking | 410 | 24.2±11.8 | 24.2±11.8 |  | NR | NR |  | NR | NR | dhhh  jf |
| Maeda, 2010{Maeda, 2011 30 /id}  21178986  Japan  NR | (i) aspirin (100 mg, q.d.), (ii) aspirin (100 mg, q.d.) plus clopidogrel (75 mg, q.d. or (iii) aspirin (100 mg, q.d.) plus ticlopidine (100 mg, b.i.d.; |  |  |  |  |  |  |  |  |  |  |  |  |  |  | Figure 2 a, box plot based on genotype, gigure 3 a, box plot based on genotype |
| Yamamoto 2011{Yamamoto, 2011 25 /id}  21168310  Japan  NR | 300mg loading dose and 75mg/day clopidogrel maintenance dose plus 100mg aspirin | CYP2C19\*1/\*1 | Platelet reactivity | Aggregation units  (AU) Min | NR | \*1/\*1 | EM 47 | 3194 | 1570 Au min | Mann-Whitney U test | NR | NR | EM vs IM  P<0.05 | NR | NR |  |
|  |  | CYP2C19\*1/\*2, \*1/\*3 | Platelet reactivity | Aggregation units  (AU) Min | NR | \*1/\*2, \*1/\*3 | IM  51 | 4184 | 1400 Au min |  | NR | NR |  | NR | NR |  |
|  |  | CYP2C19\*2/\*2, \*2/\*3, \*3/\*3 | Platelet reactivity | Aggregation units  (AU) Min | NR | \*2/\*2, \*2/\*3, \*3/\*3 | PM  25 | 5088 | 1080 Au min | Mann-Whitney U test | NR | NR | IM vs P M  P<0.05 | NR | NR |  |
|  |  | CYP2C19\*1/\*1 | Platelet reactivity | Aggregation units  (AU) Min | <7 days | \*1/\*1 | EM  25 | 3186 | 1595 Au min | Mann-Whitney U test | NR | NR | EM vs IM  P<0.05 | NR | NR |  |
|  |  | CYP2C19\*1/\*2, \*1/\*3 | Platelet reactivity | Aggregation units  (AU) Min | <7 days | \*1/\*2, \*1/\*3 | IM  32 | 3007 | 1541 Au min | Mann-Whitney U test | NR | NR |  | NR | NR |  |
|  |  | CYP2C19\*2/\*2, \*2/\*3, \*3/\*3 | Platelet reactivity | Aggregation units  (AU) Min | <7 days | \*2/\*2, \*2/\*3, \*3/\*3 | PM  12 | 4655 | 1380 Au min | Mann-Whitney U test | NR | NR | IM vs PM  P<0.05 | NR | NR |  |
|  |  | CYP2C19\*1/\*1 | Platelet reactivity | Aggregation units  (AU) Min | ≥7 days | \*1/\*1 | EM  22 | 3186 | 1595 Au min | Mann-Whitney U test | NR | NR | EM vs IM  NS | NR | NR |  |
|  |  | CYP2C19\*1/\*2, \*1/\*3 | Platelet reactivity | Aggregation units  (AU) Min | ≥7 days | \*1/\*2, \*1/\*3 | IM  19 | 3007 | 1541 Au min | Mann-Whitney U test | NR | NR |  | NR | NR |  |
|  |  | CYP2C19\*2/\*2, \*2/\*3, \*3/\*3 | Platelet reactivity | Aggregation units  (AU) Min | ≥7 days | \*2/\*2, \*2/\*3, \*3/\*3 | PM  13 | 4655 | 1380 Au min | Mann-Whitney U test | NR | NR | IM vs PM  P<0.05 | NR | NR |  |
| Sibbing, 2010{Sibbing, 2010 48 /id}  20492469  Germany | Aspirin and clopidogrel (75 mg/day) | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*2 (wt/wt) | 738 | 212 | NR | Kruskal-Wallis test | NR | 141-351 | P=0.0001 for \*2/\*2 vs wt/wt | No | NR | Figure 2a and b, bootstrap results |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*2 (wt/\*2) | 229 | 305 |  |  |  | 162-482 | P=0.01 for \*2/\*2 vs wt/\*2 patients |  |  |  |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*2 (\*2/\*2) | 19 | 475 |  |  |  | 387-575 |  |  |  |  |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*17 (wt/wt) | 608 | 243 |  | Kruskal-Wallis test |  | 151-416 | P=0.007 for \*17/\*17 vs wt/wt | No | NR |  |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*17 (wt/\*17) | 335 | 217 |  |  |  | 141-375 | P=0.06 for \*17/\*17 vs wt/\*17 patients |  |  |  |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*17 (\*17/\*17) | 43 | 164 |  |  |  | 120-273 |  |  |  |  |
|  |  | **Genetic Test Used [index test]** | **Reactivity Outcome** | **Outcome Definition** | **Timing of measurement** | **Index test result: category (e.g., EM) – ONE ROW PER GENOTYPE GROUP** | **No. with given genotype** | **Platelet reactivity measurement for the genotype group**  **[metric]**  **Median** | **SD/SE (report value and metric)** | **Statistical method** | **Mean difference (state if other metric)** | **95% CI of mean difference (state if other metric)** | **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)** |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*17+/\*2- | 319 | 207 | NR | Kruskal-Wallis test | NR | 132-332 | P<0.001 for  CYP2C19 \*17+/\*2-  Vs  CYP2C19 \*17-/\*2+ | NR | NR |  |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*17+/\*2- | 419 | NR | NR | Kruskal-Wallis test | NR |  | No | NR | NR |  |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*17+/\*2+ | 59 | NR | NR | Kruskal-Wallis test | NR |  | No | NR |  |  |
|  |  | CYP2C19 | Platelet aggregation | Aggregation measured with MEA is quantified as aggregation units(AU) and area under the curve(AUC) of aggregation units (AU\*min). | NR | CYP2C19 \*17-/\*2+ | 189 | 309 | NR | Kruskal-Wallis test | NR | 172-490 | No | NR |  |  |
| Bouman 2011{Bouman, 2011 9 /id}  21628721  Netherlands  Genetic substudy of the Popular study | pretreated with clopidogrel (75 mg daily for >5 days, or a loading dose of 300 mg ≥24 h or 600 mg ≥4 h before (PCI)) and aspirin (80-100 mg daily ≥10 days prior to PCI) Clopidogrel and aspirin maintenance doses were 75 mg and 80 to 100 mg daily, respectively. | CYP2C19 genetic test (real-time PCR) | On-treatment platelet reactivity | 5 umol/l ADP-induced LTA | Within 2 hr after blood sampling | CYP2C19\*2 heterozygotes | 260 | 44% aggregation | SD 14% | ANOVA) followed by the least signiﬁcant difference post-hoc test | NR | NR | NR | 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 volume, clopidogrel regimen, PPI use, and amlodipine use) | NR |  |
|  |  |  |  | 20 umol/l ADP-induced LTA |  |  |  | 63% aggregation | SD 13% |  |  |  |  |  |  |  |
|  |  |  |  | Plateletworks assay |  |  |  | 72% aggregation | SD 27% |  |  |  |  |  |  |  |
|  |  |  |  | VerifyNow P2Y12 |  |  |  | 230 platelet reactivity units (PRU) | SD 27 PRU |  |  |  |  |  |  |  |
|  |  |  |  | 5 umol/l ADP-induced LTA |  | CYP2C19\*2 homozygotes | 27 | 52% aggregation | SD 14% |  |  |  |  |  |  |  |
|  |  |  |  | 20 umol/l ADP-induced LTA |  |  |  | 70% aggregation | SD 9% |  |  |  |  |  |  |  |
|  |  |  |  | Plateletworks assay |  |  |  | 90% aggregation | SD 21% |  |  |  |  |  |  |  |
|  |  |  |  | VerifyNow P2Y12 |  |  |  | 257 platelet reactivity units (PRU) | SD 60 PRU |  |  |  |  |  |  |  |
|  |  |  |  | 5 umol/l ADP-induced LTA |  | CYP2C19\*2 noncarrier | 737 | 38% aggregation | SD 14% |  |  |  |  |  |  |  |
|  |  |  |  | 20 umol/l ADP-induced LTA |  |  |  | 56% aggregation | SD 15% |  |  |  |  |  |  |  |
|  |  |  |  | Plateletworks assay |  |  |  | 61% aggregation | SD 30% |  |  |  |  |  |  |  |
|  |  |  |  | VerifyNow P2Y12 |  |  |  | 202 platelet reactivity units (PRU) | SD 76 PRU |  |  |  |  |  |  |  |
| Campo 2011{Campo, 2011 13 /id}  21679849  Italy  NR | aspirin (300 mg as loading dose [LD and MD 100 mg daily, Clopidogrel 600 mg LD , clopidogrel 75 mg/day was continued for 12 months. | TaqMan | Platelet reactivity | VerifyNow values | Baseline (before PCI) | \*2 noncarriers | 219 | Mean 181 PRU | SD 97 PRU | t test and  1-way analysis of variance | NR | NR | see table 2 | linear mixed model | baseline, genetic, and procedural characteristics | Data are from Table 2. Some P values there are not yet reported here because I can’t tell what comparison they’re for |
|  |  |  |  |  |  | \*2 heterozygote | 76 | Mean 216 PRU | SD 92 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*2 homozygote | 5 | Mean 236 PRU | SD 112 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*2 carrier | 81 | Mean 216 PRU | SD 91 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  | 1 mo after PCI | \*2 noncarriers | 219 | Mean 133 PRU | SD  81 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 heterozygote | 76 | Mean 182 PRU | SD 88 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*2 homozygote | 5 | Mean 221 PRU | SD 105 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*2 carrier | 81 | Mean 185 PRU | SD 90 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  | 6 mo after PCI | \*2 noncarriers | 204 | Mean 132 PRU | SD  81 PRU |  |  |  |  |  |  | Ns are less at 6 mo because data for this time point only available for 281 pts |
|  |  |  |  |  |  | \*2 heterozygote | 73 | Mean 180 PRU | SD 85 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*2 homozygote | 4 | Mean 218 PRU | SD 95 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*2 carrier | 77 | Mean 183 PRU | SD 87 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  | Baseline (before PCI) | \*17 noncarriers | 198 | Mean 203 PRU | SD  92 PRU | t test and  1-way analysis of variance | NR | NR | see table 2 |  |  | Data are from Table 2. Some P values there are not yet reported here because I can’t tell what comparison they’re for |
|  |  |  |  |  |  | \*17 heterozygote | 85 | Mean 171 PRU | SD 100 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*17 homozygote | 17 | Mean 139 PRU | SD 100 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*17 carrier | 102 | Mean 165 PRU | SD 101 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  | 1 mo after PCI | \*17 noncarriers | 198 | Mean 163 PRU | SD  83 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*17 heterozygote | 85 | Mean 122 PRU | SD 79 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*17 homozygote | 17 | Mean 88 PRU | SD 88 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*17 carrier | 102 | Mean 117 PRU | SD 81 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  | 6 mo after PCI | \*17 noncarriers | 185 | Mean 163 PRU | SD  81 PRU |  |  |  |  |  |  | Ns are less at 6 mo because data for this time point only available for 281 pts |
|  |  |  |  |  |  | \*17 heterozygote | 79 | Mean 119 PRU | SD 83 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*17 homozygote | 17 | Mean 88 PRU | SD 93 PRU |  |  |  | <0.05 vs noncarrier |  |  |  |
|  |  |  |  |  |  | \*17 carrier | 96 | Mean 113 PRU | SD 85 PRU |  |  |  |  |  |  |  |
| Fernando 2011{Fernando, 2011 233 /id}  21696537  Australia  NR | clopidogrel 75 mg daily and randomized to either esomeprazole 40 mg or placebo (sugar ﬁlled) capsule daily for a period of 6 weeks and routine aspirin (100 mg). followed by a 2-week wash-out . Patients then resumed clopidogrel 75 mg daily and the opposite therapy . | GenesFx (PCR) | Mean change in platelet reactivity from baseline | VASP data (PRI units) | After treatment (first or second) or washout, but otherwise NR | Poor/intermediate metabolizers | 6 | Mean | SEM | Two-way ANOVA | NR | NR | <0.01 vs. row below [Two-way ANOVA] | NR | NR | Get data from Fig 4—either report data for esomeprazole and placebo treatment separately or average? |
|  |  |  |  |  |  | Extensive metabolizers | 23 |  |  |  |  |  |  |  |  |  |
|  |  |  |  | Aggregometry data (AUC units) |  | Poor/intermediate metabolizers | 6 |  |  |  |  |  | <0.01 vs. row below [Two-way ANOVA] |  |  |  |
|  |  |  |  |  |  | Extensive metabolizers | 23 |  |  |  |  |  |  |  |  |  |
|  |  |  |  | VerifyNow (PRU) data |  | Poor/intermediate metabolizers | 6 |  |  |  |  |  | <0.01 vs. row below [Two-way ANOVA] |  |  |  |
|  |  |  |  |  |  | Extensive metabolizers | 23 |  |  |  |  |  |  |  |  |  |
| Geisler 2008  18781853  Germany  NR |  | MassARRAY for \*2 | Residual platelet aggregation (RPA) | From turbidometry | Post-clopidogrel loading dose | \*2/\*2 | 10 | Median RPA 54% | NR | NR | NR | NR | NR | NR | NR | NO |
|  |  |  |  |  |  | \*1/\*2 | 52 | Median RPA, 46% |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 175 | Median RPA, 30% |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*17/\*17 | 21 | Median RPA 37% |  |  |  |  | NS for this and next two rows |  |  |  |
|  |  |  |  |  |  | \*1/\*17 | 79 | Median RPA, 30% |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 137 | Median RPA, 36% |  |  |  |  |  |  |  |  |
| Gladding 2008{Gladding, 2008 149 /id}  19463375  New Zealand  PRINC (Plavix Response in Coronary Intervention) Trial | All patients: 600-mg clopidogrel at the start of the PCI procedure. At 2 hours after, 37 patients received 600 mg clopidogrel and 23 received placebo. Starting the next day, all patients were separately randomized to receive clopidogrel 75 or 150 mg once daily for 1 week, followed by 75 mg once daily thereafter. | TaqMan PCR | Platelet inhibition (% of baseline) | VerifyNow data | At 2 hr | CYP2C19\*1\*1 homozygotes | 24 | Median (range) 23 (0% to 66%) | NR | NR | NR | NR | 0.0295 (vs. row below)  [Mann-Whitney U test] | NO | NO | Raw data in Fig 3 |
|  |  |  |  |  |  | CYP2C19\*2 or \*4 carriers | 19 | Median (range) 10% (0% to 56%) |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 carriers | 17 | Median (range) 9% (0% to 98%) |  |  |  |  | 0.0262 (vs. 2 rows above)  [Mann-Whitney U test] |  |  |  |
|  |  |  |  |  | At 4 hr | CYP2C19\*1\*1 homozygotes receiving 1200 mg total | 15 | Median (range) 43% (13% to 97%) | NR | NR | NR | NR | 0.3 (vs. row below)  [Mann-Whitney U test] | NO | NO | Raw data in Fig 4 |
|  |  |  |  |  |  | CYP2C19\*1\*1 homozygotes receiving 600 mg total | 9 | Median (range) 35% (0% to 65%) |  |  |  |  |  |  |  |  |
|  |  |  |  |  | At 7 hr | CYP2C19\*1\*1 homozygotes receiving 1200 mg total | 15 | Median (range) 63% (15% to 98%) | NR | NR | NR | NR | 0.05(vs. row below)  [Mann-Whitney U test] | NO | NO | Raw data in Fig 4 |
|  |  |  |  |  |  | CYP2C19\*1\*1 homozygotes receiving 600 mg total | 9 | Median (range) 29% (0% to 75%) |  |  |  |  |  |  |  |  |
|  |  |  |  |  | At 7 days | CYP2C19\*1\*1 homozygotes receiving 150 mg daily | 12 | Median (range) 46% (18% to 97%) | NR | NR | NR | NR | 0.2 (vs. row below)  [Mann-Whitney U test] | NO | NO | Raw data in Fig 4 |
|  |  |  |  |  |  | CYP2C19\*1\*1 homozygotes receiving 75 mg daily | 6 | Median (range) 32% (24% to 64%) |  |  |  |  |  |  |  |  |
|  |  |  |  |  | At 4 hours | CYP2C19\*2 or \*4 carriers receiving 1200 mg total | 11 | Median (range) 37% (8% to 87%) |  |  |  |  | 0.002 (vs. row below)  [Mann-Whitney U test] |  |  | Raw data in Fig 5 |
|  |  |  |  |  |  | CYP2C19\*2 or \*4 carriers receiving 600 mg total | 8 | Median (range) 14% (0% to 22%) |  |  |  |  |  |  |  |  |
|  |  |  |  |  | At 7 hours | CYP2C19\*2 or \*4 carriers receiving 1200 mg total | 11 | Median (range) 42% (7% to 94%) |  |  |  |  | 0.09 (vs. row below)  [Mann-Whitney U test] |  |  | Raw data in Fig 5 |
|  |  |  |  |  |  | CYP2C19\*2 or \*4 carriers receiving 600 mg total | 8 | Median (range) 22% (0% to 51%) |  |  |  |  |  |  |  |  |
|  |  |  |  |  | At 7 days | CYP2C19\*2 or \*4 carriers receiving 150 mg daily | 5 | Median (range) 51% ( 15% to 86%) |  |  |  |  | 0.042 (vs. row below)  [Mann-Whitney U test] |  |  | Raw data in Fig 5 |
|  |  |  |  |  |  | CYP2C19\*2 or \*4 carriers receiving 75 mg daily | 9 | Median (range) 14% (0% to 67%) |  |  |  |  |  |  |  |  |
|  |  |  |  |  | At 7 hours | CYP2C9\*1/\*3 heterozygotes receiving 600 mg total | NR but something’s wrong—“None of the patients carried the CYP2C19\*3 allele.” | Median (range) 9% (8% to 11%) |  |  |  |  | 0.045 (vs. row below)  [Mann-Whitney U test] |  |  |  |
|  |  |  |  |  |  | CYP2C9\*1/\*1 homozygotes receiving 600 mg total | 9 | Median (range) 31% (0% to 96%) |  |  |  |  |  |  |  |  |
| Gurbel 2010{Gurbel, 2010 91 /id}  19817997  USA  NR | 75 mg clopidogrel daily | TaqMan | 5uM ADP-induced platelet aggregation (%) | NR | Pre-elinogrel | CYP2C19\*2 carrier | 17 | 52 ± 13%  Mean±SD | NR | NR | NR | NR | 0.001 vs. row below [one-way ANOVA] | NR | NR | NO |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 19 | 36 ± 14%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | 20 uM ADP-induced platelet aggregation (%) |  | Pre-elinogrel | CYP2C19\*2 carrier | 17 | 61 ± 12%  Mean±SD | NR | NR | NR | NR | 0.03 vs. row below [one-way ANOVA] | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 19 | 50 ± 13%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | VASP assay platelet reactivity index |  | Pre-elinogrel | CYP2C19\*2 carrier | 17 | 72 ± 12 PRI  Mean±SD | NR | NR | NR | NR | 0.05 vs. row below [one-way ANOVA] | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 19 | 58 ± 20 PRI  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | VerifyNow P2Y12 assay-platelet reactivity units |  | Pre-elinogrel | CYP2C19\*2 carrier | 17 | 259 ± 68 PRU  Mean±SD | NR | NR | NR | NR | 0.14 vs. row below [one-way ANOVA] | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 19 | 214 ± 82 PRU  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | VerifyNow P2Y12 assay-percent inhibition |  | Pre-elinogrel | CYP2C19\*2 carrier | 17 | 19 ± 19%  Mean±SD | NR | NR | NR | NR | 0.07 vs. row below [one-way ANOVA] | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 19 | 35 ± 24%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | TEG-ADP-induced platelet-ﬁbrin clot strength (mm) |  | Pre-elinogrel | CYP2C19\*2 carrier | 17 | 57 ± 8 mm  Mean±SD | NR | NR | NR | NR | 0.18 vs. row below [one-way ANOVA] | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 19 | 49 ± 12 mm  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | TEG-percent inhibition |  | Pre-elinogrel | CYP2C19\*2 carrier | 17 | 23 ± 9%  Mean±SD | NR | NR | NR | NR | 0.07 vs. row below [one-way ANOVA] | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 19 | 36 ± 20%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | Change in 5 mM ADP-induced platelet aggregation (%) | Change in % aggregration between baseline and 4 hours in the 17 patients with HPR at baseline | Pre vs post-elinogrel | CYP2C19\*2 carrier | 14 | see fig 12 | NR | NR | NR | NR | 0.0001 vs. row below[one-way ANOVA] | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarrier | 3 | see fig 12 |  |  |  |  |  |  |  |  |
|  |  |  | 5 mM ADP-induced platelet aggregation (%) |  | Pre-elinogrel | CYP2C19\*17 noncarrier | 15 | 41 ± 19%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 21 | 45 ± 14%  Mean±SD | NR | NR | NR | NR | 0.30 vs. row above [one-way ANOVA] | NR | NR |  |
|  |  |  | 20 mM ADP-induced platelet aggregation (%) | 20 mM ADP-induced platelet aggregation (%) | Pre-elinogrel | CYP2C19\*17 noncarrier | 15 | 51 ± 14%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 21 | 58 ± 13%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  | VASP assay-platelet reactivity index | VASP assay-platelet reactivity index | Pre-elinogrel | CYP2C19\*17 noncarrier | 15 | 60 ± 23 PRI  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 21 | 67 ± 15 PRI  Mean±SD | NR | NR | NR | NR | 0.35 vs. row above [one-way ANOVA] | NR | NR |  |
|  |  |  | VerifyNow P2Y12 assay-platelet reactivity units | VerifyNow P2Y12 assay-platelet reactivity units | Pre-elinogrel | CYP2C19\*17 noncarrier | 15 | 206 ± 91 PRU Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 21 | 251 ± 65 PRU  Mean±SD | NR | NR | NR | NR | 0.13 vs. row above [one-way ANOVA] | NR | NR |  |
|  |  |  | VerifyNow P2Y12 assay-per cent inhibition | VerifyNow P2Y12 assay-per cent inhibition | Pre-elinogrel | CYP2C19\*17 noncarrier | 15 | 35 ± 28%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 21 | 24 ± 18%  Mean±SD | NR | NR | NR | NR | 0.24 vs. row above [one-way ANOVA] | NR | NR |  |
|  |  |  | TEG-ADP-induced platelet-ﬁbrin clot strength (mm) | TEG-ADP-induced platelet-ﬁbrin clot strength (mm) | Pre-elinogrel | CYP2C19\*17 noncarrier | 15 | 51 ± 12 mm  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 21 | 53 ± 11 mm  Mean±SD | NR | NR | NR | NR | 0.83 vs. row above [one-way ANOVA] | NR | NR |  |
|  |  |  | TEG-percent inhibition | TEG-percent inhibition | Pre-elinogrel | CYP2C19\*17 noncarrier | 15 | 35 ± 28%  Mean±SD |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarrier | 21 | 24 ± 18%  Mean±SD | NR | NR | NR | NR | 0.17 vs. row above [one-way ANOVA] | NR | NR |  |
| Kim 2011{Kim, 2011 18 /id}  21511217  South Korea  CCELAMI2C19 | 600-mg (LD) of clopidogrel, followed (MD) of 75 mg daily before randomization. All patients also took a 300-mg LD of aspirin, followed by aspirin 200 mg daily throughout the study period. After blood sampling pre-discharge, the patients were randomly assigned to high-MD clopidogrel of 150 mg daily (high-dose group) or adjunctive cilostazol 100 mg twice daily to clopidogrel 75 mg daily (standard dose + cilostazol group). | PCR and SNaPshot assay kit | LTA maximal platelet aggregation | 20 mmol/l ADP | Pre-discharge | \*2 or \*3 noncarrier | 24 | Mean 54.1% | SD 16.1% | Student unpaired t or  Mann-Whitney U test | NR | NR | 0.293 vs. corresponiding cilostazol row below | NO | NO | NONE |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 60.0% | SD 15.2% |  |  |  | 0.802 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 24 | Mean 38.6% | SD 12.0% |  |  |  | 0.752 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 52.3% | SD 17.5% |  |  |  | <0.001 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | Absolute change between baseline and 30 days | \*2 or \*3 noncarrier | 24 | Mean 15.5% | SD 15.1% |  |  |  | 0.197 vs. corresponiding cilostazol row below |  |  | Data are also in Fig. 2 |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 7.7% | SD 15.5% |  |  |  | <0.001 vs. corresponiding cilostazol row below |  |  |  |
|  | 600-mg (LD) of clopidogrel, followed (MD) of 75 mg daily before randomization. All patients also took a 300-mg LD of aspirin, followed by aspirin 200 mg daily throughout the study period. After blood sampling pre-discharge, the patients were randomly assigned to high-MD clopidogrel of 150 mg daily (high-dose group) or adjunctive cilostazol 100 mg twice daily to clopidogrel 75 mg daily (standard dose + cilostazol group). | PCR and SNaPshot assay kit | LTA maximal platelet aggregation | 20 mmol/l ADP | Pre-discharge | \*2 or \*3 noncarrier | 25 | Mean 58.4% | SD 11.9% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 59.2% | SD 14.4% |  |  |  |  |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 25 | Mean 37.5% | SD 13.2% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 35.0% | SD 19.3% |  |  |  |  |  |  |  |
|  |  |  |  | Absolute change between baseline and 30 days |  | \*2 or \*3 noncarrier | 25 | Mean 20.9% | SD 13.9% |  |  |  |  |  |  | Data are also in Fig. 2 |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 24.2% | SD 17.2% |  |  |  |  |  |  |  |
|  | High-dose clopidogrel | PCR and SNaPshot assay kit | LTA maximal platelet aggregation | 5 umol/l ADP | Pre-discharge | \*2 or \*3 noncarrier | 24 | Mean 42.4% | SD 15.7% |  |  |  | 0.256 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 46.6% | SD 16.7% |  |  |  | 0.995 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 24 | Mean 30.1% | SD 10.1% |  |  |  | 0.547 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 37.6% | SD 16.0% |  |  |  | <0.001 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  | Absolute change between baseline and 30 days |  | \*2 or \*3 noncarrier | 24 | Mean 12.3% | SD 13.8% |  |  |  | 0.094 vs. corresponiding cilostazol row below |  |  | Data are also in Fig. 2 |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 9.0% | SD 13.3% |  |  |  | <0.001 vs. corresponiding cilostazol row below |  |  |  |
|  | Standar-dose clopidogrel + cilostazol | PCR and SNaPshot assay kit | LTA maximal platelet aggregation | 5 umol/l ADP | Pre-discharge | \*2 or \*3 noncarrier | 25 | Mean 46.9% | SD 11.8% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 46.6% | SD 15.6% |  |  |  |  |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 25 | Mean 28.2% | SD 11.5% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 24.9% | SD 14.3% |  |  |  |  |  |  |  |
|  |  |  |  | Absolute change between baseline and 30 days |  | \*2 or \*3 noncarrier | 25 | Mean 18.8% | SD 12.5% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 |  |  |  |  |  |  |  |  |  |
|  | High-dose clopidogrel | PCR and SNaPshot assay kit | LTA late platelet aggregation | 20 umol/l ADP | Pre-discharge | \*2 or \*3 noncarrier | 24 | Mean 44.4% | SD 22.7% |  |  |  | 0.379 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 50.9% | SD 21.7% |  |  |  | 0.878 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 24 | Mean 21.8% | SD 40.6% |  |  |  | 0.649 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 40.6% | SD 22.2% |  |  |  | 0.001 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  | Absolute change between baseline and 30 days |  | \*2 or \*3 noncarrier | 24 | Mean 22.6% | SD 19.6% |  |  |  | 0.211 vs. corresponiding cilostazol row below |  |  | Data are also in Fig. 3 |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 10.3% | SD 20.9% |  |  |  | <0.001 vs. corresponiding cilostazol row below |  |  |  |
|  | Standar-dose clopidogrel + cilostazol | PCR and SNaPshot assay kit | LTA late platelet aggregation | 20 mmol/l ADP | Pre-discharge | \*2 or \*3 noncarrier | 25 | Mean 49.4% | SD 15.7% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 51,.6% | SD 17.7% |  |  |  |  |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 25 | Mean 19.7% | SD 16.8% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 23.5% | SD 19.2% |  |  |  |  |  |  |  |
|  |  |  |  |  | Absolute change between baseline and 30 days | \*2 or \*3 noncarrier | 25 | Mean 29.6% | SD 19.3% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 28.1% | SD 19.4% |  |  |  |  |  |  |  |
|  | High-dose clopidogrel | PCR and SNaPshot assay kit | LTA late platelet aggregation | 5 mmol/l ADP | Pre-discharge | \*2 or \*3 noncarrier | 24 | Mean 32.5% | SD 18.2% |  |  |  | 0.397 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 38.4% | SD 20.7% |  |  |  | 0.749 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 24 | Mean 16.4% | SD 9.2% |  |  |  | 0.347 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 26.7% | SD 16.5% |  |  |  | <0.001 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | Absolute change between baseline and 30 days | \*2 or \*3 noncarrier | 24 | Mean 16.0% | SD 16.2% |  |  |  | 0.144 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 11.7% | SD 15.2% |  |  |  | <0.001 vs. corresponiding cilostazol row below |  |  |  |
|  | Standar-dose clopidogrel + cilostazol | PCR and SNaPshot assay kit | LTA late platelet aggregation | 5 mmol/l ADP LTA | Pre-discharge | \*2 or \*3 noncarrier | 25 | Mean 36.4% | SD 13.5% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 39.8% | SD 17.4% |  |  |  |  |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 25 | Mean 13.6% | SD 11.7% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 15.2% | SD 12.4% |  |  |  |  |  |  |  |
|  |  |  |  |  | Absolute change between baseline and 30 days | \*2 or \*3 noncarrier | 25 | Mean 22.8% | SD 15.6% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 24.6% | SD 15.4% |  |  |  |  |  |  |  |
|  | High-dose clopidogrel | PCR and SNaPshot assay kit | VerifyNow platelet reactivity | VerifyNow platelet reactivity | Pre-discharge | \*2 or \*3 noncarrier | 24 | Mean 245.0 PRU | SD 91.6 PRU |  |  |  | 0.959 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 241.6 PRU | SD 79.3 PRU |  |  |  | 0.220 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 24 | Mean 152.2 PRU | SD 70.4 PRU |  |  |  | 0.441 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 184.2 PRU | SD 80.6 PRU |  |  |  | 0..518 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  | Absolute change between baseline and 30 days | Change between pre-discharge and 30 days after discharge | \*2 or \*3 noncarrier | 24 | Mean 92.8 PRU | SD 60.7 PRU |  |  |  | 0..347 vs. corresponiding cilostazol row below |  |  | Data are also in Fig. 5 |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 57.3 PRU | SD 69.4 PRU |  |  |  | 0.060 vs. corresponiding cilostazol row below |  |  |  |
|  | Standar-dose clopidogrel + cilostazol | PCR and SNaPshot assay kit | VerifyNow platelet reactivity | VerifyNow platelet reactivity | Pre-discharge | \*2 or \*3 noncarrier | 25 | Mean 246.2 PRU | SD 76.3 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 263.0 PRU | SD 72.5 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 25 | Mean 136.6 PRU | SD 70.0 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 171.9 PRU | SD 86.3 PRU |  |  |  |  |  |  |  |
|  |  |  |  | Absolute change between baseline and 30 days |  | \*2 or \*3 noncarrier | 25 | Mean 109.6 PRU | SD 63.1 PRU |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 91.1 PRU | SD 85.0 PRU |  |  |  |  |  |  |  |
|  | High-dose clopidogrel | PCR and SNaPshot assay kit | VerifyNow % inhiibition |  | Pre-discharge | \*2 or \*3 noncarrier | 24 | Mean 26.2% | SD 25.0% |  |  |  | 0..672 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 22.0% | SD 19.2% |  |  |  | 0.825 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 24 | Mean 54.7% | SD 22.3% |  |  |  | 0.783 vs. corresponiding cilostazol row below |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 38 | Mean 40.3% | SD 23.5% |  |  |  | 0.157 vs. corresponiding cilostazol row below |  |  |  |
|  | Standar-dose clopidogrel + cilostazol | PCR and SNaPshot assay kit | VerifyNow % inhibition |  | Pre-discharge | \*2 or \*3 noncarrier | 25 | Mean 23.5% | SD 18.9% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 21.1% | SD 16.8% |  |  |  |  |  |  |  |
|  |  |  |  |  | At 30 days | \*2 or \*3 noncarrier | 25 | Mean 56.4% | SD 20.7% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 or \*3 carrier | 39 | Mean 48.0% | SD 24.0% |  |  |  |  |  |  |  |
| Lee 2011{Lee, 2011 4 /id}  21786436  South Korea  NR | 75 mg clopidogrel daily for at least six days before platelet testing | Seeplex CYP2C19 ACE Genotyping system | VerifyNow P2Y12 reactivity units (clopidogrel resistance) | VerifyNow P2Y12 reactivity units (clopidogrel resistance) | NR | Extensive CYP2C19 metabolizers | 68 | 195.0 PRU mean | 84.9 PRU  SD | analysis of variance (ANOVA) test and post hoc analysis | NR | NR | *p*<0.001 among this and next two rows  [ANOVA] | NR | NR | Post hoc analysis using the Bonferroni test showed significant differences between all subgroups |
|  |  |  |  |  |  | Intermediate metabolizers | 74 | 237.9 PRU  mean | 88.0 PRU SD |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Poor metabolizers | 24 | 302.2  PRU  mean | 58.9 PRU SD |  |  |  |  |  |  |  |
|  |  |  | percent inhibition | percent inhibition | NR | Extensive CYP2C19 metabolizers | 68 | 44.6% mean | 21.8% SD |  |  |  | *p*<0.001 among this and next two rows  [ANOVA] |  |  | Post hoc analysis using the Bonferroni test showed significant differences between all subgroups |
|  |  |  |  |  |  | Intermediate metabolizers | 74 | 30.5%mean | 21.5% SD |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Poor metabolizers | 24 | 14.0  mean | 13.4% SD |  |  |  |  |  |  |  |
| Malek 2008{Malek, 2008 167 /id}  18577829  Poland  NR | LD 300 mg of aspirin and MD 75 mg and LD 300 or 600 mg of clopidogrel and MD 75 mg daily | PFA-100 | Median CADP-CT value | NR | Median 6 days after starting clopidogrel | Group 1 | 7 | 95 s (IQR 59–124 s) | NR | NR | NR | NR | 0.002 vs. controls (Wilcoxon rank-sum test) | NR | NR | NR |
|  |  |  |  |  |  | Group 2 | 14 | 210 s (IQR 115–300 s) |  |  |  |  | 0.01 vs. Group 1 (Wilcoxon rank-sum test), NS vs. controls and group 3 |  |  |  |
|  |  |  |  |  |  | Group 3 | 17 | 286 s (IQR 108–300 s) |  |  |  |  | 0.01 vs. Group 1 (Wilcoxon rank-sum test), NS vs. controls and group 2 |  |  |  |
|  |  |  |  |  |  | Controls | 67 | 289 s (IQR 182–300 s) |  |  |  |  | NA |  |  |  |
| Pettersen 2011{Pettersen, 2011 228 /id}  21426546  Norway  Aspirin and Clopidogrel non-responsiveness clinical Endpoint Trial (ASCET) | 75 mg/day clopidogrel; also possibly aspirin but details NR | TaqMan Drug Metabolism Assay | Platelet reactivity | VASP | one month | CYP2C19\*2 carrier | 64 | 51% Mean platelet reactivity index value | NR | NR | NR | NR | < 0.001 vs. row below (either Student ’s unpaired t-test or Mann-Whitney U-test) | NO | NO | NONE |
|  |  |  |  |  |  | \*2 noncarrier | 104 | 38% Mean platelet reactivity index value |  |  |  |  |  |  |  |  |
|  |  |  |  | VerifyNow | one month | \*2 carrier | 64 | 162 Mean platelet reactivity units |  |  |  |  | < 0.001 vs. row below (either Student ’s unpaired t-test or Mann-Whitney U-test) |  |  |  |
|  |  |  |  |  |  | \*2 noncarrier | 104 | 121 Mean platelet reactivity units |  |  |  |  |  |  |  |  |
| Sibbing 2011{Sibbing, 2011 2 /id}  21527445  Germany  NR | loading dose of 600 mg of clopidogrel | TaqMan assay | Platelet aggregation value | ADP-induced | NR | \*2 carrier (\*1/\*2 or \*2/\*2) | 377 | Median (range)  286 (186 – 460) AU × min | NR | NR | NR | NR | 0.0001 vs. row below [Kruskal – Wallis  test] | NR | NR | Data in this table are for PCI cohort (n=5124) |
|  |  |  |  |  |  | \*2 noncarrier | 1147 | Median (range)  208 (134 – 329) AU × min |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 32 | Median (range)  208 (134–329) AU × min |  |  |  |  | 0.001 for this and next three rows [multivariable linear regression] | YES [all baseline variables] |  | 10th, 25th, 75th, and 90th percentiles are in Fig 2 |
|  |  |  |  |  |  | \*1/\*2 | 345 | Median (range)  267 (175 – 428) AU × min |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 | 1147 | Median (range)  494 (341 – 732) AU × min |  |  |  |  |  |  |  |  |
| Hwang  2010{Hwang, 2010 55 /id}  20823393  Korea  ACCEL | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 5 umol/L ADP LTA | procedural | wild type homozygote | 22 | mean  47.7 | 16.4 | t-test | NR | NR | 0.600 comparing the following group | NR | NR | figure 2-5 are bar graphs. |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 50.2 | 15.8 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 5 umol/L ADP LTA | 30 days | wild type homozygote | 22 | mean  31.1 | 12.9 | t-test | NR | NR | 0.304 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 26.7 | 15.2 |  | NR | NR |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 5 umol/L ADP LTA | procedural | mutant- type homozygote | 43 | mean  54 | 15.1 | t-test | NR | NR | 0.949 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 42.9 | 18.1 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 5 umol/L ADP LTA | 30 days | mutant type homozygote | 43 | mean  42.9 | 18.1 | t-test | NR | NR | <0.001 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 28.4 | 13.9 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 20 umol/L ADP LTA | procedural | wild type homozygote | 22 | mean  60.5 | 15.1 | t-test | NR | NR | 0.661 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 62.4 | 13.8 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 20umol/L ADP LTA | 30 days | wild type homozygote | 22 | mean  41.9 | 16.4 | t-test | NR | NR | 0.276 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 36.0 | 19.2 |  | NR | NR |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 5 umol/L ADP LTA | procedural | mutant- type homozygote | 43 | mean  66.8 | 11.3 | t-test | NR | NR | 0.99 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 66.8 | 12.2 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | maximal platelet aggregation | 5 umol/L ADP LTA | 30 days | mutant type homozygote | 43 | mean  55.4 | 15.9 | t-test | NR | NR | <0.001 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 40.5 | 16.7 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 5 umol/L ADP LTA | procedural | wild type homozygote | 22 | mean  40.3 | 20.3 | t-test | NR | NR | 0.913 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 41.0 | 17.9 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 5 umol/L ADP LTA | 30 days | wild type homozygote | 22 | mean  19.0 | 13.4 | t-test | NR | NR | 0.318 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 14.9 | 13.4 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 5 umol/L ADP LTA | procedural | mutant- type homozygote | 43 | mean  47.1 | 20.1 | t-test | NR | NR | 0.742 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 45.8 | 16.8 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 5 umol/L ADP LTA | 30 days | mutant type homozygote | 43 | mean  30.7 | 22.2 | t-test | NR | NR | <0.001 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 16.7 | 11.5 |  | NR | NR |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 20 umol/L ADP LTA | procedural | wild type homozygote | 22 | mean  52.2 | 21.1 | t-test | NR | NR | 0.734 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 54.2 | 18.4 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 20umol/L ADP LTA | 30 days | wild type homozygote | 22 | mean  26.9 | 18.8 | t-test | NR | NR | 0.321 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 21.2 | 19.0 |  | NR | NR |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 5 umol/L ADP LTA | procedural | mutant- type homozygote | 43 | mean  61.0 | 16.8 | t-test | NR | NR | 0.986 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 60.9 | 16.0 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | late platelet aggregation | 5 umol/L ADP LTA | 30 days | mutant type homozygote | 43 | mean  43.2 | 22.0 | t-test | NR | NR | <0.001 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 26.4 | 17.4 |  | NR | NR |  |  |  |  |
|  | **Treatment** | **Genetic Test Used [index test]** | **Reactivity Outcome** | **Outcome Definition** | **Timing of measurement** | **Index test result: category (e.g., EM) – ONE ROW PER GENOTYPE GROUP** | **No. with given genotype** | **Platelet reactivity measurement for the genotype group**  **[metric]** | **SD/SE (report value and metric)** | **Statistical method** | **Mean difference (state if other metric)** | **95% CI of mean difference (state if other metric)** | **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)** |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | procedural | wild type homozygote | 22 | mean  272.5 | 75.5 | t-test | NR | NR | 0.42 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 253.8 | 76.7 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | 30 days | wild type homozygote | 22 | mean  149.7 | 65.4 | t-test | NR | NR | 0.348 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 129.4 | 76.4 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | procedural | mutant- type homozygote | 43 | mean  278.3 | 69.7 | t-test | NR | NR | 0.167 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 296.5 | 53.2 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | 30 days | mutant type homozygote | 43 | mean  214.1 | 68.5 | t-test | NR | NR | 0.153 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 191.6 | 78.4 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | procedural | wild type homozygote | 22 | mean  20.2 | 18.7 | t-test | NR | NR | 0.733  comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 22.4 | 22.9 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | 30 days | wild type homozygote | 22 | mean  65.2 | 12.8 | t-test | NR | NR | 0.317comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 22 | mean 70.5 | 7.6 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | procedural | mutant- type homozygote | 43 | mean  14.0 | 16.2 | t-test | NR | NR | 0.319comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 11.1 | 10.8 |  | NR | NR |  |  |  |  |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily | CYP2C19\*2 (rs4244285.c.681G>A)  CYP2C19\*3  (rs4986893,c.636G>A) | VerifyNow PRU | P2Y12 reaction unit | 30 days | mutant type homozygote | 43 | mean  33.5 | 19.2 | t-test | NR | NR | 0.005 comparing the following group | NR | NR | no |
|  | clopidogrel therapy (75 mg +aspirin, 200 mg daily  +cilostazol |  |  |  |  |  | 47 | mean 45.8 | 21.2 |  | NR | NR |  |  |  |  |
| Cuisset, 2011{Cuisset, 2011 18195 /id}  21803320  France  NR | LD clopidogrel 600mgand aspirin 250mg, low responders received higher 150 mg MD clopidogrel | CYP2C19\*2(rs4244285) | PRI VASP mean response | PRI VASP mean response | after LD clopidogrel | CYP2C19\*2 carrier | 46/86 | mean response 66 | 10 | t-test | NR | NR | 0.58  comparing with non-carriers | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 non carrier | 105/260 | mean response 67 | 11 |  |  |  |  |  |  |  |
| Cuisset, 2011{Cuisset, 2011 18195 /id}  21803320  France  NR | LD clopidogrel 600mgand aspirin 250mg, low responders received higher 150 mg MD clopidogrel | CYP2C19\*2(rs4244285) | PRI VASP mean response | PRI VASP mean response | 1 month | CYP2C19\*2 carrier | 46/86 | mean response 57 | 14 | t-test | NR | NR | 0.01  comparing with non-carriers | NR | NR |  |
|  |  |  |  |  |  | CYP2C19\*2 non carrier | 105/260 | mean response 50 | 16 |  |  |  |  |  |  |  |
| Harmsze, 2012{Harmsze, 2012 18224 /id}  22228204  Netherlands  NR | Clopidogrel | Real-time PCR | % Reactivity on LTA |  | After PCI | \*17/\*17 | 33 | Mean % 32.2 | SD 23.1 | NR | -6.3 (vs. \*1/\*1) | -8.7 to -0.3 | Vs. \*1/\*1 row: 0.043 for mean difference; 0.048 for mean reactivity; <0.0001 across this and next 5 rows for mean reactivity [ANOVA, with least-significant-difference test] | YES (sex, age, BMI, current smoking, eGFR <60ml/min, clopidogrel loading dose, coumarin use) | NR |  |
|  |  |  |  |  |  | \*1/\*17 | 207 | Mean % 33.9 | SD 23..9 |  | -5.7(vs. \*1/\*1) | -9.6 to -1.8 | Vs. \*1/\*1 row: 0.004 for mean difference; 0.011 for mean reactivity  [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 351 | Mean % 39.2 | SD 23.6 |  | NA | NA | NA |  |  |  |
|  |  |  |  |  |  | \*2/\*17 | 47 | Mean % 49.5 | SD 24.0 |  | 9.7 (vs. \*1/\*1) | 2.8-16.6 | Vs. \*1/\*1 row: 0.006 for mean difference; <0.0001 for mean reactivity  [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | \*1/\*2 | 157 | Mean % 48.8 | SD 22.8 | ANOVA | 9.8 (vs. \*1/\*1) | 5.5-14.0 | Vs. \*1/\*1 row: <0.0001 for mean difference; 0.005 for mean reactivity [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | \*2/\*2 | 25 | Mean % 64.3 | SD 12.5 | ANOVA | 21.9 (vs. \*1/\*1) | 12.6-31.2 | Vs. \*1/\*1 row: 0.004 for mean difference; <0.0001 for mean reactivity  [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | Ultrarapid metabolizer (\*1 or \*17/\*17) | 240 | NR | NR | ANOVA | -5.6 (vs. extensive) | -9.6 to -2.1 | 0.002  [ANOVA, with least-significant-difference test] | YES (see above) |  |  |
|  |  |  |  |  |  | Extensive metabolizer (\*1/\*1) | 351 | NR | NR |  | NA | NA | NA |  |  |  |
|  |  |  |  |  |  | Intermediate/poor metabolizer (\*2/\*1, \*2, or \*17) | 229 | NR | NR | ANOVA | 11.1 (vs. extensive) | 7.3-14.9 | <0.0001  [ANOVA, with least-significant-difference test] | YES (see above) |  |  |
| Harmsze, 2012{Harmsze, 2012 18224 /id}  22228204  Netherlands  NR | Clopidogrel | Real-time PCR | PRU on VerifyNow | NR | After PCI | \*17/\*17 | 33 | Mean PRU 189 | SD 79 | ANOVA | -17 (vs. \*1/\*1) | -42 to 7.7 | Vs. \*1/\*1 row: 0.17 for mean difference and 0.08 for mean reactivity  Also <0.0001 across this and next 5 rows for mean reactivity [ANOVA, with least-significant-difference test] | YES (sex, age, BMI, current smoking, eGFR <60ml/min, clopidogrel loading dose, coumarin use) | NR |  |
|  |  |  |  |  |  | \*1/\*17 | 207 | Mean PRU 196 | SD 79 | ANOVA | -14 (vs. \*1/\*1) | -26 to -1.3 | Vs. \*1/\*1 row: 0.031for mean difference and 0.047 for mean reactivity  [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | \*1/\*1 | 351 | Mean PRU 208 | SD 74 |  | NA | NA | NA |  |  |  |
|  |  |  |  |  |  | \*2/\*17 | 47 | Mean PRU 234 | SD 74 | ANOVA | 24 (vs. \*1/\*1) | 2.4-46 | Vs. \*1/\*1 row: 0.030 for mean difference and <0.0001 for mean reactivity  [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | \*1/\*2 | 157 | Mean PRU 233 | SD 72 | ANOVA | 24 (vs. \*1/\*1) | 11-38 | Vs. \*1/\*1 row: <0.0001 for mean difference and <0.0001 for mean reactivity  [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | \*2/\*2 | 25 | Mean PRU 254 | SD 62 | ANOVA | 38 (vs. \*1/\*1) | 8.8-66 | Vs. \*1/\*1 row: 0.011 for mean difference and 0.003 for mean reactivity  [ANOVA, with least-significant-difference test] |  |  |  |
|  |  |  |  |  |  | Ultrarapid metabolizer (\*1 or \*17/\*17) | 240 | NR | NR | ANOVA | -14 (vs. extensive) | -26 to -2.4 | 0.018  [ANOVA, with least-significant-difference test] | YES (see above) |  |  |
|  |  |  |  |  |  | Extensive metabolizer (\*1/\*1) | 351 |  |  |  | NA | NA | NA |  |  |  |
|  |  |  |  |  |  | Intermediate/poor metabolizer (\*2/\*1, \*2, or \*17) | 229 |  |  | ANOVA | 26 (vs. extensive) | 14-38 | <0.0001  [ANOVA, with least-significant-difference test] | YES (see above) |  |  |
| Gajos, 2012{Gajos, 2012 18197 /id}  22623230  Poland  OMEGA-PCI | LD clopidogrel 600mg and MD 75mg daily+75 mg aspirin daily | CYP2C19\*1/\*1 | LTA ADP 5uM platelet aggregation | LTA ADP 5uM platelet aggregation | 3-5 days | placebo | 30 | mean 46.8 | SD 14.1 | NR | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | 30 days |  |  | mean 48.1 | SD10.6 |  |  |  |  |  |  |  |
|  | LD clopidogrel 600mg and MD 75mg daily+75 mg aspirin daily | CYP2C19\*1/\*1 | LTA ADP 20uM platelet aggregation | LTA ADP 20uM platelet aggregation | 3-5 days | placebo | 30 | mean  54.3 | SD  17.9 | NR | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | 30 days |  |  | mean 54.7 | SD 10.6 |  |  |  |  |  |  |  |
| Gajos, 2012{Gajos, 2012 18197 /id}  22623230  Poland  OMEGA-PCI | LD clopidogrel 600mg and MD 75mg daily+75 mg aspirin daily | CYP2C19\*1/\*2 and \*2/\*2 | LTA ADP 5uM platelet aggregation | LTA ADP 5uM platelet aggregation | 3-5 days | placebo | 30 | mean 49.9 | SD 9.7 | NR | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | 30 days |  |  | mean 55.2 | SD  11.6 |  |  |  |  |  |  |  |
|  | LD clopidogrel 600mg and MD 75mg daily+75 mg aspirin daily | CYP2C19\*1/\*2 and \*2/\*2 | LTA ADP 5uM platelet aggregation | LTA ADP 20uM platelet aggregation | 3-5 days | placebo | 30 | mean  61.4 | SD  10.7 | NR | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | 30 days |  |  | mean 60.2 | SD 9.7 |  |  |  |  |  |  |  |
| Kreutz, 2012{Kreutz, 2012 18223 /id}  22427735  US  NR | Clopidogrel | PCR | Maximal platelet aggregation | By LTA, 5 μmol/L ADP | Within 24 hr | \*2 carrier | 44 | Mean 37.9 | SD 12 | NR | NR | NR | Univariate linear regression, 0.037  Multivariate, 0.04  Vs. next row | YES for multivariate regression, “clinical variables that are known to affect platelet reactivity and response to clopidogrel and variables with P < 0.1 in univariate analysis” [not otherwise specified] | NR | Simiilar results per genotype, not just carrier status (i.e., for \*1/\*1, \*1/\*2, and \*2/\*2) given in Fig. 1; could be digitized |
|  |  |  |  |  |  | \*2 noncarrier | 107 | Mean 29.9 | SD 11.2 |  |  |  |  |  |  |  |
|  |  |  |  |  | 4 hr | \*2 carrier in PCI subgroup | 14 | NR | NR | NR | NR | NR | 0.25 vs. next row [Kruskal-Wallis]  Also P=0.1 for mean change from baseline | NR | NR | Means and SEMs given in Fig. 4; could be digitized |
|  |  |  |  |  |  | \*2 noncarrier in PCI subgroup | 28 | NR | NR | NR | NR | NR |  |  |  |  |
|  |  |  |  |  | 16-24 hr | \*2 carrier in PCI subgroup | 14 | NR | NR | NR | NR | NR | 0.35 vs. next row [Kruskal-Wallis] Also P=0.13 for mean change from baseline |  |  | Means and SEMs given in Fig. 4; could be digitized |
|  |  |  |  |  |  | \*2 noncarrier in PCI subgroup | 28 | NR | NR | NR | NR | NR |  |  |  |  |
|  |  |  |  | By LTA, 10 μmol/L ADP |  | \*2 carrier | 44 | Mean 45.0 | SD 13.1 |  |  |  | Univariate linear regression, 0.034  Multivariate, 0..036  Vs. next row |  |  |  |
|  |  |  |  |  |  | \*2 noncarrier | 107 | Mean 36.2 | SD 14.3 |  |  |  |  |  |  |  |
|  |  |  |  |  | 4 hr | \*2 carrier in PCI subgroup | 14 | NR | NR | NR | NR | NR | 0.23 vs. next row [Kruskal-Wallis] Also P=0.03 for mean change from baseline | NR | NR | Means and SEMs given in Fig. 4; could be digitized |
|  |  |  |  |  |  | \*2 noncarrier in PCI subgroup | 28 | NR | NR | NR | NR | NR |  |  |  |  |
|  |  |  |  |  | 16-24 hr | \*2 carrier in PCI subgroup | 14 | NR | NR | NR | NR | NR | 0.23 vs. next row [Kruskal-Wallis] Also P=0.04 for mean change from baseline |  |  | Means and SEMs given in Fig. 4; could be digitized |
|  |  |  |  |  |  | \*2 noncarrier in PCI subgroup | 28 | NR | NR | NR | NR | NR |  |  |  |  |
|  |  |  |  | By LTA, 20 μmol/L ADP |  | \*2 carrier | 44 | Mean 51.3 | SD 11 |  |  |  | Univariate linear regression, 0.034  Multivariate, 0.034  Vs. next row |  |  |  |
|  |  |  |  |  |  | \*2 noncarrier | 107 | Mean 43.6 | SD 12 |  |  |  |  |  |  |  |
|  |  |  |  |  | 4 hr | \*2 carrier in PCI subgroup | 14 | NR | NR | NR | NR | NR | 0.49 vs. next row [Kruskal-Wallis] Also P=0.14for mean change from baseline | NR | NR | Means and SEMs given in Fig. 4; could be digitized |
|  |  |  |  |  |  | \*2 noncarrier in PCI subgroup | 28 | NR | NR | NR | NR | NR |  |  |  | dhdhd |
|  |  |  |  |  | 16-24 hr | \*2 carrier in PCI subgroup | 14 | NR | NR | NR | NR | NR | 0.27 vs. next row [Kruskal-Wallis] Also P=0.09 for mean change from baseline |  |  | Means and SEMs given in Fig. 4; could be digitized |
|  |  |  |  |  |  | \*2 noncarrier in PCI subgroup | 28 | NR | NR | NR | NR | NR |  |  |  |  |
|  |  |  |  | VerifyNow PRU |  | \*2 carrier | 44 | Mean 234.6 | SD 67 |  |  |  | Univariate linear regression, 0.027  Multivariate, 0.014  Vs. next row |  |  |  |
|  |  |  |  |  |  | \*2 noncarrier | 107 | Mean 195.0 | SD 78 |  |  |  |  |  |  |  |
|  |  |  |  | VerifyNow % inhibition |  | \*2 carrier | 44 | Mean 12.9 | SD 14 |  |  |  | Univariate linear regression, 0.013  Multivariate, 0.012  Vs. next row |  |  |  |
|  |  |  |  |  |  | \*2 noncarrier | 107 | Mean 27.7 | SD 25 |  |  |  |  |  |  |  |
| Tello-Montoliu 2012{Tello-Montoliu, 2012 18200 /id}  22116003  Spain  study one of the paper | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*2 | LTA ADP platelet aggregation | LTA ADP 5uM | in hospital | G/G | 31 | mean 47.1 | SD 14.3 | t-test | NR | NR | 0.19  comparing with the next row | NR | NR |  |
|  |  |  |  |  |  | \*/A | 9 | mean 54.2 | SD 12.5 |  |  |  |  |  |  |  |
|  | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*2 | LTA ADP platelet aggregation | LTA ADP 10uM | in hospital | G/G | 31 | mean 54.2 | SD 15.5 | t-test | NR | NR | 0.17  comparing with the next row | NR | NR |  |
|  |  |  |  |  |  | \*/A | 9 | mean 62.6 | SD 17.4 |  |  |  |  |  |  |  |
|  | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*17 | LTA ADP platelet aggregation | LTA ADP 5uM | in hospital | C/C | 27 | mean 50.3 | SD 14.6 | t-test | NR | NR | 0.319  comparing with the next row | NR | NR |  |
|  |  |  |  |  |  | \*/T | 13 | mean 45.5 | SD 12.8 |  |  |  |  |  |  |  |
|  | 100mg AA and 75mg MD clopidogrel | CYP2C19 \*17 | LTA ADP platelet aggregation | LTA ADP 10uM | in hospital | C/C | 27 | mean 58.1 | SD 16.4 | t-test | NR | NR | 0.265  comparing with the next row | NR | NR |  |
|  |  |  |  |  |  | \*/T | 13 | mean 51.9 | SD 15.4 |  |  |  |  |  |  |  |
| Dai, 2012{Dai, 2012 18226 /id}  22704413  China  NR | Clopidogrel and aspirin | PCR-RFLP | Mean late inhibition (%) | Inhibition 5 min after addition of agonist, thought to reflect clopidogrel action better than max. inhibition | Baseline | \*17/\*17 (n=6) | 6 | Mean 46.32 | SD 8.79 | NR | NR | NR | <0.01 vs wild type/wild type  [ANOVA and SNK-q (?) test] | NR | NR | Table 3 also reports max. aggregation, max. inhibition, and disaggregation. |
|  |  |  |  |  |  | \*17/wild type (n=71) | 71 | Mean 39.68 | SD 8.26 |  |  |  | <0.01 vs wild type/wild type  [ANOVA and SNK-q (?) test] |  |  |  |
|  |  |  |  |  |  | Wild type/wild type (n=443) | 443 | Mean 26.77 | SD 9.18 |  |  |  |  |  |  |  |
|  |  |  | Mean late aggregation (%) | Aggregation 5 min after addition of agonist, thought to reflect clopidogrel action better than max. inhibition | Baseline | \*17/\*17 (n=6) | 6 | Mean 47.55 | SD 9.54 |  |  |  | NS vs wild type/wild type  [ANOVA and SNK-q (?) test] |  |  |  |
|  |  |  |  |  |  | \*17/wild type (n=71) | 71 | Mean 47.45 | SD 11.98 |  |  |  | NS vs wild type/wild type  [ANOVA and SNK-q (?) test] |  |  |  |
|  |  |  |  |  |  | Wild type/wild type (n=443) | 443 | Mean 48.92 | SD 35.87 |  |  |  |  |  |  |  |
|  |  |  | Mean late aggregation (%) | Aggregation 5 min after addition of agonist, thought to reflect clopidogrel action better than max. inhibition | 10 days | \*17/\*17 (n=6) | 6 | Mean 24.87 | SD 8.20 |  |  |  | <0.05 vs wild type/wild type  [ANOVA and SNK-q (?) test] |  |  |  |
|  |  |  |  |  |  | \*17/wild type (n=71) | 71 | Mean 29.12 | SD 9.75 |  |  |  | <0.01 vs wild type/wild type  [ANOVA and SNK-q (?) test] |  |  |  |
|  |  |  |  |  |  | Wild type/wild type (n=443) | 443 | Mean 35.87 | SD 11.50 |  |  |  |  |  |  |  |
| Harmsze, 2011{Harmsze, 2011 18201 /id}  21854540  Netherlands  POPular | 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 | NR | -1.4 | -4.7,-0.68 | 0.039 | 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 | NR | -3.6 | -7.1,0.003 | 0.05 | 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 | NR | -2.6 | -6.8,-1.5 | 0.034 | 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 | NR | -7.0 | -10.2,-3.8 | <0.0001 | 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 | NR | -7.6 | -13.1,-2.1 | 0.007 | 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 | NR | -7.8 | -12.6,-3.0 | 0.002 | 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 | NR | -10 | -16.1,-3.9 | 0.001 | NR | NR |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Harmsze, 2011{Harmsze, 2011 18201 /id}  21854540  Netherlands  POPular | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 20uM | LTA ADP  high on-treatment reactivity | in hospital | CCB+, PPI-, \*2 - | HOPR+ | NR | NR | NR | -3.6 | -6.7,-0.56 | 0.02 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 20uM | LTA ADP  high on-treatment reactivity | in hospital | CCB-, PPI+, \*2 - | HOPR+ | NR | NR | NR | -3.8 | -7.4,-0.31 | 0.033 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 20uM | LTA ADP  high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 - | HOPR+ | NR | NR | NR | -7.7 | -12.5,-2.9 | 0.002 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 20uM | LTA ADP  high on-treatment reactivity | in hospital | CCB-, PPI-, \*2+ | HOPR+ | NR | NR | NR | -8.0 | -10.9,-5.1 | <0.0001 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 20uM | LTA ADP  high on-treatment reactivity | in hospital | CCB+, PPI-, \*2+ | HOPR+ | NR | NR | NR | -11 | -16.9,-5.2 | <0.0001 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 20uM | LTA ADP  high on-treatment reactivity | in hospital | CCB-, PPI+, \*2+ | HOPR+ | NR | NR | NR | -11.3 | -15.6,-7.1 | <0.0001 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | LTA-ADP 20uM | LTA ADP  high on-treatment reactivity | in hospital | CCB+, PPI+, \*2 + | HOPR+ | NR | NR | NR | -11.6 | -19.5, -2.9 | 0.008 | NR | NR |  |
| Harmsze, 2011{Harmsze, 2011 18201 /id}  21854540  Netherlands  POPular | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | verifynow | verifynow P2Y12 | in hospital | CCB+, PPI-, \*2 - | HOPR+ | NR | NR | NR | -8.0 | -16,-0.06 | 0.013 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | verifynow | verifynow P2Y12 | in hospital | CCB-, PPI+, \*2 - | HOPR+ | NR | NR | NR | -18 | -34,-2.2 | 0.026 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | verifynow | verifynow P2Y12 | in hospital | CCB+, PPI+, \*2 - | HOPR+ | NR | NR | NR | -42 | -67,-17 | 0.001 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | verifynow | verifynow P2Y12 | in hospital | CCB-, PPI-, \*2+ | HOPR+ | NR | NR | NR | -30 | -45,-15 | <0.0001 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | verifynow | verifynow P2Y12 | in hospital | CCB+, PPI-, \*2+ | HOPR+ | NR | NR | NR | -50 | -71,-28 | <0.0001 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | verifynow | verifynow P2Y12 | in hospital | CCB-, PPI+, \*2+ | HOPR+ | NR | NR | NR | -53 | -83,-23 | 0.001 | NR | NR |  |
|  | clopidogrel LD 600 mg and 75mg/d >5 days+  aspirin 80-100 mg day | CYP2C19 \*2 | verifynow | verifynow P2Y12 | in hospital | CCB+, PPI+, \*2 + | HOPR+ | NR | NR | NR | -70 | -113,-27 | 0.001 | NR | NR |  |
| Ono, 2011{Ono, 2011 18202 /id}  21862109  Japan  NR | clopidogrel LD 300mgand 75mg MD  aspirin 100mg/day | CYP2C19 | LTA | LTA | in hospital | carrier of reduced function allel | 20uM ADP-PR max | mean 57 | 10.4 | t-test | NR | NR | <0.001 comparing with the next row  t-test | NR | NR | NR |
|  |  |  |  |  |  | non- carrier of reduced function allel |  | mean 48.5 | 12 |  |  |  |  |  |  |  |
|  | clopidogrel LD 300mgand 75mg MD  aspirin 100mg/day | CYP2C19 | LTA | LTA | in hospital | carrier of reduced function allel | 20uM ADP-PR area | mean 4306 | 1389 | t-test | NR | NR | <0.001 comparing with the next row  t-test | NR | NR | NR |
|  |  |  |  |  |  | non- carrier of reduced function allel |  | mean 2960 | 1740 |  |  |  |  |  |  |  |
|  | clopidogrel LD 300mgand 75mg MD  aspirin 100mg/day | CYP2C19 | Verifynow | Verifynow | in hospital | carrier of reduced function allel | P2Y12 reaction Unit | mean 290 | 81.2 | t-test | NR | NR | <0.001 comparing with the next row  t-test | NR | NR | NR |
|  |  |  |  |  |  | non- carrier of reduced function allel |  | mean 217.6 | 82.4 |  |  |  |  |  |  |  |
|  | clopidogrel LD 300mgand 75mg MD  aspirin 100mg/day | CYP2C19 | Verifynow | Verifynow | in hospital | carrier of reduced function allel | inhibition | mean 17.9 | 17.8 | t-test | NR | NR | <0.001 comparing with the next row  t-test | NR | NR | NR |
|  |  |  |  |  |  | non- carrier of reduced function allel |  | mean 35.5 | 22.8 |  |  |  |  |  |  |  |
| Fontana 2011 {Fontana, 2011 18211 /id}  21692977  Switzerland  ADRIE | aspirin and 75 mg clopidogrel | CYP2C19\*1 and \*2 | VASP | vasodilator-stimulated phosphoprotein | 1 month | non-carrier of \*2 | 368 | mean 46% PRI | NR | NR | NR | IQR 33-57 | 0.0001  NR | NR | NR | NR |
|  |  |  |  |  |  | carrier of one\*2 | 151 | mean 58%PRI |  |  |  | IQR 48-69 |  |  |  |  |
|  |  |  |  |  |  | carrier of two \*2 | 17 | mean  78% PRI |  |  |  | IQR  68-75 |  |  |  |  |
|  | aspirin and 75 mg clopidogrel | CYP2C19\*1 and \*2 | LTA ADP | light transmission aggregometer | 1 month | non-carrier of \*2 | 366 | mean 55% | NR | NR | NR | IQR 45-63 | 0.011  NR | NR | NR | NR |
|  |  |  |  |  |  | carrier of one\*2 | 152 | mean 62% |  |  |  | IQR 56-70 |  |  |  |  |
|  |  |  |  |  |  | carrier of two \*2 | 17 | mean  66% |  |  |  | IQR  54-72 |  |  |  |  |
| Kreutz, 2012{Kreutz, 2012 18218 /id}  22385219  USA  NR | Clopidogrel and aspirin | Real-time PCR | Mean maximal platelet aggregation, ADP 20 micromol as agonist | By LTA | 15 days | \*1/\*1 | 68 | 43.6% | 12% | Unpaired 2-sided test (Student’s t if normally distributed and Wilcoxon rank sum if not, but article doesn’t say) | NR | NR | 0.005 vs. next row | NR | NR | NONE |
|  |  |  | Mean maximal platelet aggregation, ADP 20 micromol as agonist |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) | 28 | 51% | 11% |  | NR | NR | NA | NR | NR | NONE |
|  |  |  | Mean maximal platelet aggregation, ADP 20 micromol + PGE1 22 nM as agonists |  |  | \*1/\*1 | 68 | 17.7% | 13% |  | NR | NR | 0.002 vs. next row | NR | NR | NONE |
|  |  |  | Mean maximal platelet aggregation, ADP 20 micromol + PGE1 22 nM as agonists |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) | 28 | 27.9% | 14% |  | NR | NR | NA | NR | NR | NONE |
|  |  |  | Mean maximal platelet aggregation, ADP 20 micromol + PGE1 88 nM as agonists |  |  | \*1/\*1 | 68 | 6.7% | 13% |  | NR | NR | 0.01 vs. next row | NR | NR | NONE |
|  |  |  | Mean maximal platelet aggregation, ADP 20 micromol + PGE1 88 nM as agonists |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) | 28 | 13.9% | 14% |  | NR | NR | NA | NR | NR | NONE |
|  |  |  | Mean PRU | By VerifyNow |  | \*1/\*1 | 68 | 195 PRU | 78 PRU |  | NR | NR | 0.017 vs. next row | NR | NR | NONE |
|  |  |  | Mean PRU |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) | 28 | 234.6 PRU | 67 PRU |  | NR | NR | NA | NR | NR | NONE |
| Marcucci, 2012{Marcucci, 2012 18217 /id}  22390861  Italy  NR | Clopidogrel and aspirin | Allelic discrimination assay | Mean maximal platelet aggregation, ADP 10 micromol | By LTA | 12 mo | \*1/\*1 | 892 | 46.8% | 21.7% | NR | NR | NR | <0.0001 vs. next row (Student’s t or Mann-Whitney U) | NR | NR | NONE |
|  |  |  |  |  | 12 mo | \*2 carrier (\*2/\*2 or \*2/\*1) | 295 | 52.5% | 19.9% | NR | NR | NR | NA | NR | NR | NONE |
|  |  |  |  |  | 12 mo | \*1/\*1 | 892 | AUC 0.66 | 95% CI 0.57-0.75 | NR | NR | NR | <0.001 | NR | NR | Fig. 2 reports data for this row identical to next row, but text reports the data recorded here |
|  |  |  |  |  | 12 mo | \*2 carrier (\*2/\*2 or \*2/\*1) | 295 | AUC 0.64 | 95% CI 0.57-0.71 | NR | NR | NR | <0.001 | NR | NR | NONE |
| Mega, 2011{Mega, 2011 18190 /id}  22088980  USA  ELEVATE-TIMI 56 | 75 mg clopidogrel daily | Pyrosequencing and Nanosphere Verigene | Mean VASP PRI | NR | Any time within 2-week treatment period for this dose | \*1/\*1 | 237 | 57.5% | 55.1-59.9% | NR | NR | NR | <0.001 for trend, across this and all \*1/\*1 data in subsequent rows (different doses) [mixed model] | Time from sample collection to analysis | Tukey-Kramer correction | From Fig 2 and Table 2 |
|  |  |  |  |  |  | \*2/\*1 | 75 | 70.0% | 66.0-74.0% |  |  |  | <0.001 for trend, across this and all \*2/\*1 data in subsequent rows (different doses) [mixed model] |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 86.6% | 80.7-92.5% |  |  |  | 0.003 for trend, across this and all \*2/\*2 data in subsequent rows (different doses) [mixed model] |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 80 | 71.0 | 67.1-74.9 |  |  |  | <0.001 for trend, across this and all \*2 carriers data in subsequent rows (different doses) [mixed model] |  |  |  |
|  | 150 mg daily |  |  |  |  | \*1/\*1 | 232 | 46.9% | 44.3-49.1% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*1 | 75 | 61.4% | 57.0-65.9% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 77.8% | 67.4-88.1% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 80 | 62.4% | 58.1-66.7% |  |  |  |  |  |  |  |
|  | 225 mg clopidogrel daily |  |  |  |  | \*2/\*1 | 76 | 52.7% | 48.0-57.4% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 73.0% | 50.6-95.5% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 81 | 54.0% | 49.4-58.5% |  |  |  |  |  |  |  |
|  | 300 mg clopidogrel daily |  |  |  |  | \*2/\*1 | 75 | 48.9% | 44.6-53.2% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 68.3% | 44.9-91.6% |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 81 | 50.1% | 45.9-54.3% |  |  |  |  |  |  |  |
|  | 75 mg clopidogrel daily |  | Mean VerifyNow PRU | NR | Any time within 2-week treatment period for this dose | \*1/\*1 | 236 | 163.6 | 154.4-173.9 | NR | NR | NR | <0.001 for trend, across this and all \*1/\*1 data in subsequent rows (different doses) [mixed model] | Time from sample collection to analysis | Tukey-Kramer correction | From Fig 2 and Table 2 |
|  |  |  |  |  |  | \*2/\*1 | 76 | 225.6 | 207.7-243.4 |  |  |  | <0.001 for trend, across this and all \*2/\*1 data in subsequent rows (different doses) [mixed model] |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 328.8 | 247.9-409.7 |  |  |  | 0.32 for trend, across this and all \*2/\*2 data in subsequent rows (different doses) [mixed model] |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 81 | 231.9 | 214.0-249.8 |  |  |  | <0.001 for trend, across this and all \*2 carriers data in subsequent rows (different doses) [mixed model] |  |  |  |
|  | 150 mg daily |  |  |  |  | \*1/\*1 | 230 | 126.7 | 117.7-137.5 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*1 | 73 | 188.1 | 170.8-205.4 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 310.2 | 247.5-372.9 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 78 | 195.9 | 178.2-213.7 |  |  |  |  |  |  |  |
|  | 225 mg clopidogrel daily |  |  |  |  | \*2/\*1 | 75 | 152.9 | 135.2-170.6 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 286.0 | 177.9-394.1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 80 | 161.2 | 142.6-179.8 |  |  |  |  |  |  |  |
|  | 300 mg clopidogrel daily |  |  |  |  | \*2/\*1 | 73 | 127.5 | 109.9-145.2 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 (n=6) | 5 | 287.0 | 170.2-403.8 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2 carrier (\*2/\*2 or \*2/\*1) (n=86) | 78 | 137.7 | 118.4-157.1 |  |  |  |  |  |  |  |
| Park, 2012{Park, 2012 18216 /id}  22507978  Korea  ACCEL-STATIN | At least 6 mo daily maintenance clopidogrel and aspirin | TaqMan | Mean maximal platelet aggregation | By LTA with 20 micromol ADP | Baseline | \*2 or \*3 carriage | 30 | 68.2% | SD 8.7% | NR | Beta coefficient 5.3 | SE 2.6 | 0.057 for %, vs. next row  [Student’s unpaired t or Mann-Whitney U and ANOVA]  0.055 for beta | NR | NR | NONE |
|  |  |  |  |  |  | \*1\*1 | 15 | 63.2% | SD 7.0% |  |  |  |  |  |  |  |
|  |  |  |  | By LTA with 5 micromol ADP |  | \*2 or \*3 carriage | 30 | 54.5% | SD 11.0% |  |  |  | 0.075 vs. next row [Student’s unpaired t or Mann-Whitney U and ANOVA] |  |  |  |
|  |  |  |  |  |  | \*1\*1 | 15 | 48.6% | SD 8.4% |  |  |  |  |  |  |  |
|  |  |  | Mean final platelet aggregation | By LTA with 20 micromol ADP |  | \*2 or \*3 carriage | 30 | 61.6% | SD 12.8% |  |  |  | 0.027vs. next row [Student’s unpaired t or Mann-Whitney U and ANOVA] |  |  |  |
|  |  |  |  |  |  | \*1\*1 | 15 | 52.1% | SD 13.7% |  |  |  |  |  |  |  |
|  |  |  |  | By LTA with 5 micromol ADP |  | \*2 or \*3 carriage | 30 | 44.8% | SD 15.2% |  |  |  | 0.044 vs. next row [Student’s unpaired t or Mann-Whitney U and ANOVA] |  |  |  |
|  |  |  |  |  |  | \*1\*1 | 15 | 35.6% | SD 11.3% |  |  |  |  |  |  |  |
|  |  |  | PRU | By VerifyNow with 20 micromol ADP |  | \*2 or \*3 carriage | 30 | 296 | SD 68 |  |  |  | 0.561 vs. next row [Student’s unpaired t or Mann-Whitney U and ANOVA] |  |  |  |
|  |  |  |  |  |  | \*1\*1 | 15 | 284 | SD 58 |  |  |  |  |  |  |  |
|  |  |  | Percent inhibition | By VerifyNow with 20 micromol ADP |  | \*2 or \*3 carriage | 30 | 17.9% | SD 16.6% |  |  |  | 0.725 vs. next row [Student’s unpaired t or Mann-Whitney U and ANOVA] |  |  |  |
|  |  |  |  |  |  | \*1\*1 | 15 | 19.6% | SD 11.2% |  |  |  |  |  |  |  |
| Yamane, 2012{Yamane, 2012 18229 /id}  22472213  Japan  NR | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and rabeprazole | CYP2C19 | LTA ADP | maximal aggregation rates (MARs) | 2 weeks | CYP2C19 | EM N=8 | 23.9 | SD 13.8% | wilxocon matched-pairs signed-ranks test | NR | NR | 0.0547  comparingwith omeprazole treated group  wilxocon matched-pairs signed-ranks test | No | no | no |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and omeprazole | CYP2C19 | LTA ADP | maximal aggregation rates (MARs) | 2 weeks | CYP2C19 | EM N=8 | 35.6 | SD 15.2% |  |  |  |  |  |  |  |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and rabeprazole | CYP2C19 | LTA ADP | maximal aggregation rates (MARs) | 2 weeks | CYP2C19 | IM N=14 | 27.6 | SD 16.2% | wilxocon matched-pairs signed-ranks test | NR | NR | 0.0156  comparingwith omeprazole treated group  wilxocon matched-pairs signed-ranks test | No | no | no |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and omeprazole | CYP2C19 | LTA ADP | maximal aggregation rates (MARs) | 2 weeks | CYP2C19 | IM N=14 | 36.9 | 16.5 |  |  |  |  |  |  |  |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and rabeprazole | CYP2C19 | LTA ADP | maximal aggregation rates (MARs) | 2 weeks | CYP2C19 | PM N=3 | 33.7 | SD 14.7 | wilxocon matched-pairs signed-ranks test | NR | NR | NR | No | no | no |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and omeprazole | CYP2C19 | LTA ADP | maximal aggregation rates (MARs) | 2 weeks | CYP2C19 | PM N=3 | 29.8 | SD 19.3% |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Yamane, 2012{Yamane, 2012 18229 /id}  22472213  Japan  NR | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and rabeprazole | CYP2C19 | VeryfyNow P2y12 | P2Y12 reaction units (PRU) | 2-4 weeks | CYP2C19 | EM N=8 | 197.1 | SD 69.1 | wilxocon matched-pairs signed-ranks test | NR | NR | 0.0142  comparingwith omeprazole treated group  wilxocon matched-pairs signed-ranks test | No | no | no |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and omeprazole | CYP2C19 | VeryfyNow P2y12 | P2Y12 reaction units (PRU) | 2-4 weeks | CYP2C19 | EM N=8 | 251.5 | SD 59.5 |  |  |  |  |  |  |  |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and rabeprazole | CYP2C19 | VeryfyNow P2y12 | P2Y12 reaction units (PRU) | 2-4 weeks | CYP2C19 | IM N=14 | 232.9 | 78.1 | wilxocon matched-pairs signed-ranks test | NR | NR | 0.0516 comparingwith omeprazole treated group  wilxocon matched-pairs signed-ranks test | No | no | no |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and omeprazole | CYP2C19 | VeryfyNow P2y12 | P2Y12 reaction units (PRU) | 2-4 weeks | CYP2C19 | IM N=14 | 269.5 | SD 62 |  |  |  |  |  |  |  |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and rabeprazole | CYP2C19 | VeryfyNow P2y12 | P2Y12 reaction units (PRU) | 2-4 weeks | CYP2C19 | PM N=3 | 192.0 | SD 25 | wilxocon matched-pairs signed-ranks test | NR | NR | NR | No | no | no |
|  | aspirin 82-162 mg/day and 75 mg/day clopidogrel daily  and omeprazole | CYP2C19 | VeryfyNow P2y12 | P2Y12 reaction units (PRU) | 2-4 weeks | CYP2C19 | PM N=3 | 173.3 | SD 19.4 |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hsu, 2011{Hsu, 2011 18235 /id}  21144850  Taiwan  NR | esomeprazole and 75 mg or 35.5 mg/day for 2 weeks | CYP2C19\*1/ CYP2C19\*2/  CYP2C19\*3 | ADP induced platlet aggregation | PPA ( percent of platelet aggregation) | day 1 | esomeprazole-plus-clopidogrel group  hetEMs | n=7 | 34.6% | 14.6% | chi square test or Fisher’s exact test | NR | NR | 0.965 comparing with day 28 homEM | NR | NR | no |
|  |  |  |  |  |  | esomeprazole-plus-clopidogrel group  PMs | n=3 | 38% | 26.1 | chi square test or Fisher’s exact test |  |  | 0.817 comparing with day 28 homEM 7 |  |  |  |
|  |  |  |  |  |  | esomeprazole-plus-clopidogrel group  homEM | n=8 | 22% | 16% | chi square test or Fisher’s exact test |  |  | 0.229 comparing with day 28 homEM |  |  |  |
|  | esomeprazole and 75 mg or 35.5 mg/day for 2 weeks | CYP2C19\*1/ CYP2C19\*2/  CYP2C19\*3 | ADP induced platlet aggregation |  | day 28 | esomeprazole-plus-clopidogrel group  hetEMs | n=7 | 40.3% | 10.7% | chi square test or Fisher’s exact test | NR | NR | see above | NR | NR | no |
|  |  |  |  |  |  | esomeprazole-plus-clopidogrel group  PMs | n=3 | 38% | 26.1% | chi square test or Fisher’s exact test |  |  |  |  |  |  |
|  |  |  |  |  |  | esomeprazole-plus-clopidogrel group  homEM | n=8 | 27.5% | 14% | chi square test or Fisher’s exact test |  |  |  |  |  |  |
|  | clopidogrel 75 mg or 35.5 mg/day for 2 weeks | CYP2C19\*1/ CYP2C19\*2/  CYP2C19\*3 | ADP induced platlet aggregation | PPA ( percent of platelet aggregation) | day 1 | hetEMs | n=6 | 31.5% | 23.9% | chi square test or Fisher’s exact test | NR | NR | 0.512  comparing with day 28 homEM | NR | NR | no |
|  |  |  |  |  |  | PMs | n=2 | 63% | 1.4% | chi square test or Fisher’s exact test |  |  | 0.838  comparing with day 28 homEM 7 |  |  |  |
|  |  |  |  |  |  | homEM | n=12 | 24.9% | 19.7% | chi square test or Fisher’s exact test |  |  | 0.871  comparing with day 28 homEM |  |  |  |
|  | clopidogrel 75 mg or 35.5 mg/day for 2 weeks | CYP2C19\*1/ CYP2C19\*2/  CYP2C19\*3 | ADP induced platlet aggregation |  | day 28 | hetEMs | n=6 | 40.2% | 25.3% | chi square test or Fisher’s exact test | NR | NR | see above | NR | NR | no |
|  |  |  |  |  |  | PMs | n=2 | 57% | 13.1% | chi square test or Fisher’s exact test |  |  |  |  |  |  |
|  |  |  |  |  |  | homEM | n=12 | 26% | 19.3% | chi square test or Fisher’s exact test |  |  |  |  |  |  |
| Kim, 2011{Kim, 2012 18236 /id}  Korea  ACCEL-TRIPLE | cilostazol 100 mg twice a day  clopidogrel 75 mg once a day  aspirin 200mg once a day | CYP2C19 | 5uM ADP agg MAX(%) | 5uM ADP agg MAX(%) | 30 days | EM | 48 | 24.6 | 13.3 | ANOVA of the three groups  Jonckheere-Terpstra | NR | 20.8-28.5 | 0.062  ANOVA of the three groups  0.016  Jonckheere-Terpstra | NR | NR | no |
|  |  |  |  |  |  | IM | 54 | 28.7 | 12.2 |  |  | 25.4-32 |  |  |  |  |
|  |  |  |  |  |  | PM | 25 | 32.3 | 15.7 |  |  | 25.8-38.7 |  |  |  |  |
|  | cilostazol 100 mg twice a day  clopidogrel 75 mg once a day  aspirin 200mg once a day | CYP2C19 | 5uM ADP agg Late (%) | 5uM ADP agg Late(%) | 30 days | EM | 48 | 12.1 | 12.2 | ANOVA of the three groups  Jonckheere-Terpstra | NR | 8.6-15.7 | 0.021  ANOVA of the three groups  0.002  Jonckheere-Terpstra | NR | NR | no |
|  |  |  |  |  |  | IM | 54 | 16.4 | 11.1 |  |  | 13.3-19.4 |  |  |  |  |
|  |  |  |  |  |  | PM | 25 | 21 | 14 |  |  | 15.2-26.7 |  |  |  |  |
|  | cilostazol 100 mg twice a day  clopidogrel 75 mg once a day  aspirin 200mg once a day | CYP2C19 | 20uM ADP agg MAX(%) | 5uM ADP agg MAX(%) | 30 days | EM | 48 | 34.2 | 16.7 | ANOVA of the three groups  Jonckheere-Terpstra | NR | 29.3-39 | 0.007  ANOVA of the three groups  0.003  Jonckheere-Terpstra | NR | NR | no |
|  |  |  |  |  |  | IM | 54 | 41.7 | 14.2 |  |  | 37.8-45.6 |  |  |  |  |
|  |  |  |  |  |  | PM | 25 | 44.9 | 17 |  |  | 37.9-51.0 |  |  |  |  |
|  | cilostazol 100 mg twice a day  clopidogrel 75 mg once a day  aspirin 200mg once a day | CYP2C19 | 20uM ADP agg Late (%) | 5uM ADP agg Late(%) | 30 days | EM | 48 | 18.5 | 17.4 | ANOVA of the three groups  Jonckheere-Terpstra | NR | 13.4-23.5 | 0.002  ANOVA of the three groups  <0.001  Jonckheere-Terpstra | NR | NR | no |
|  |  |  |  |  |  | IM | 54 | 27.1 | 16.8 |  |  | 22.5-31.6 |  |  |  |  |
|  |  |  |  |  |  | PM | 25 | 32.9 | 18.1 |  |  | 25.4-40.4 |  |  |  |  |
|  | cilostazol 100 mg twice a day  clopidogrel 75 mg once a day  aspirin 200mg once a day | CYP2C19 | VerifyNow p2Y12 assay | VerifyNow P2Y12 assay | 30 days | EM | 48 | 125 | 76 | ANOVA of the three groups  Jonckheere-Terpstra | NR | 103-147 | <0.001  ANOVA of the three groups  <0.001  Jonckheere-Terpstra | NR | NR | no |
|  |  |  |  |  |  | IM | 54 | 188 | 75 |  |  | 168-209 |  |  |  |  |
|  |  |  |  |  |  | PM | 25 | 226 | 88 |  |  | 190-262 |  |  |  |  |
| Bonello, 2012{Bonello, 2012 18189 /id} 22285300 France NR | oral LD: 600 mg clopidogrel and 250 mg aspirin | CYP2C19 \*2 | Platelet aggregation | Platelet aggregation after clopidogrel LD measured by VASP | <24 hrs after clopidogrel LD | Carriers of atleast one \*2 allele (wt /\*2 or \*2/\*2) | 106 | Mean=59% | Sd=19% | NR | NR | NR | p=0.001  (wt/wt vs \*2/\*2)  [Student t-test] | No | NR |  |
|  |  |  |  |  |  | wild-type (wt) / wild-type (wt) | 261 | Mean=50% | Sd=24% | NR | NR | NR | NR |  |  |  |
| Hochholzer, 2011{Hochholzer, 2011 18208 /id}  21884870  NR  EXCELSIOR | 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 | Aggregation with  5 μmol/L ADP | 24 hrs | CYP2C19 \*2 carrier | NR | NR | NR | linear regression | NR | NR | <0.001  (carrier vs noncarrier) | Yes | NR | r2 for the regression =0.029 |
|  |  |  |  |  |  | Non CYP2C19 \*2 carrier | NR | NR | NR |  |  |  |  |  |  |  |
| Kreutz, 2012{Kreutz, 2012 18237 /id}  22459907  USA  NR | LD: 600 mg of clopidogrel | CYP2C19 \*2 | LTA | Aggregation with  5 μmol/L ADP | 24 hrs | CYP2C19 \*2 carrier | 16 | Mean=41.8 | Sd=18% | t-test | 2.7% | -7.5% to 12.8% | 0.87  Carrier vs noncarrierr  [t-test] | no | no |  |
|  |  |  |  |  |  | Non CYP2C19 \*2 carrier | 39 | Mean=39.1 | Sd=17% |  |  |  |  |  |  |  |
| Kassimis, 2012{Kassimis, 2012 18209 /id}  21831410  Greece  NR | 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 noncarriers  N=108 | 108 | Ls mean= 205.4 | 95% ci=180.9-229.9 | T test | −45.3 | -75.9 to ‑14.7 | 0.003  (noncarrier vs carrier)  [t test] | no | Nr |  |
|  |  |  |  |  |  | CYP2C19\*2 Carriers  N=38 | 38 | LS mean 250.7 | 95%ci=215.9-285.5 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*2 noncarriers  N=108 | 108 | Ls mean= 180.1 | 95% ci=125.1-235.1 | T test | −44.5 | -73.3 to ‑15.8 | 0.003  (noncarrier vs carrier)  [t test] | Yes (gender, age, BMI, DM, prior MI, statin, CCBs, PPIs, IIb/IIIa inhibitors, smoking and ACS indication for PC) | nr |  |
|  |  |  |  |  |  | CYP2C19\*2 Carriers  N=38 | 38 | LS mean 224.6 | 95%ci=163-286.3 |  |  |  |  |  |  |  |
|  |  | CYP2C19\*17 | Aggregation by VerifyNow | Aggregation by VerifyNow | 24-48 hours after procedure | CYP2C19\*17 noncarriers  N=nr | NR | LS mean 188.8 | 95%ci= 156.4-221.3 | T test | −14.0 | -46.1 to 18.0 | 0.4  (noncarrier vs carrier)  [t test] | no | Nr |  |
|  |  |  |  |  |  | CYP2C19\*17 Carriers  N=nr | NR | Ls mean= 202.9 | 95% ci= 172.9-232.8 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | CYP2C19\*17 noncarriers  N=nr | NR | Ls mean= 153.9 | 95% ci= 92.6-215.2 | T test | −2.9 | -33.4 to 27.6 | 0.9  (noncarrier vs carrier)  [t test] | Yes (gender, age, BMI, DM, prior MI, statin, CCBs, PPIs, IIb/IIIa inhibitors, smoking and ACS indication for PC) | nr |  |
|  |  |  |  |  |  | CYP2C19\*17 Carriers  N=nr | NR | LS mean 156.8 | 95%ci=91.7-221.9 |  |  |  |  |  |  |  |
| Chan,2012{Chan, 2012 18212 /id}  22462746  Singapore  NR | LD: 300 mg clopidogrel MD: 75 mg/d clopidogrel for 5-7 days | CYP2C19\*2 and CYP2C19\*3 | VASP PRI | PRI as measured by VASP phosphorylation | 7 days | No LOF allele (CYP2C19\*1/\*1) | NR | Median 65.4 | IQR=50.3-77.1 | Kruskal- wallis | NR | NR | P=0.003  [between no LOF, 1 LOF and 2 LOF]  [Kruskal-wallis] | no | nr |  |
|  |  |  |  |  |  | One LOF allele (heterozygous CYP2C19\*2 or \*3) | NR | Median 74 | IQR=66.9-82.7 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Two LOF allele (homoozygous CYP2C19\*2 and/or \*3) | NR | Median 80.3 | IQR=73.5-83.7 |  |  |  |  |  |  |  |
|  |  | CYP2C19\*17 | VASP PRI | PRI as measured by VASP phosphorylation | 7 days | Homogygous wild type(CYP2C19\*1/\*1) | NR | Median 73.9 | IQR=63.8-80.3 | Kruskal- wallis | NR | NR | P=0.001  [wild type vs variant]  [Kruskal-wallis] | no | nr |  |
|  |  |  |  |  |  | heterozygous CYP2C19\*17 | NR | Median 58 | IQR=44.7-77.4 |  |  |  |  |  |  |  |
|  |  | CYP2C19 diplotypes based on \*2, \*3 and \*17 and P, N and R status – see below  (P=\*2/non\*17 or \*3-non\*17; N=\*1-non\*17; R=\*1-\*17) |  |  |  | Poor metabolizer: P/P, N/P | 49 | Median 74.7 | IQR=68.8-83.1 | Kruskal- wallis | NR | NR | P=0.001  [wild type vs variant]  [Kruskal-wallis] | no | nr |  |
|  |  |  |  |  |  | normal metabolizer: N/N, P/R | 35 | Median 66.7 | IQR=51.8-77.3 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | rapid metabolizer: N/R,R/R | 3 | Median 50.7 | IQR=42.7-65.4 |  |  |  |  |  |  |  |
| Rideg, 2011{Rideg, 2011 18210 /id}  21806387  Hungary  DOSER | LD: 600 mg clopidogrel & 300 mg aspirin  Randomized to 4 weeks of 75 or 150 mg clopidogrel  MD: 75 mg clopidogrel/day | CYP2C19 \*1, \*2, \*3 and \*17 | Aggregation max | LTA | 24 hrs | GOF/GOF | 28 | Mean 20.1 | Sd 5.2 | Kruskal- wallis | NR | NR | P=0.02  [across all groups ]  [Kruskal-wallis] | no | nr |  |
|  |  |  |  |  |  | Wt/GOF | 41 | Mean 26.1 | Sd 13.4 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Wt/wt | 75 | Mean 27.9 | Sd 14.8 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Wt/LOF  GOF/LOF | 41 | Mean 31.7 | Sd 13.4 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | LOF/LOF | 4 | Mean 45.2 | Sd 11.8 |  |  |  |  |  |  |  |
|  |  | CYP2C19 \*1, \*2, \*3 and \*17 | VASP PRI | VASP | 24 hrs | GOF/GOF | 28 | Mean 44 | Sd 22.5 | Kruskal- wallis | NR | NR | P=0.11  [across all groups ]  [Kruskal-wallis] | no | nr |  |
|  |  |  |  |  |  | Wt/GOF | 41 | Mean 51.6 | Sd 23.2 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Wt/wt | 75 | Mean 46.7 | Sd 20.4 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | Wt/LOF  GOF/LOF | 41 | Mean 57.1 | Sd 22 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | LOF/LOF | 4 | Mean 61.8 | Sd 5.9 |  |  |  |  |  |  |  |
| Jeong, 2011{Jeong, 2011 18207 /id}  22045970  Korea  NR | LD: 600 mg clopidogrel & 300 mg aspirin  MD: 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 Aggregation maximum | Max aggregation with 5 μmol/L ADP-Aggmax | 3 days | 1/\*1 | 104 | Mean 41.9 | Sd 15.7 | ANOVA | NR | NR | P=0.031  [across all groups ]  [ANOVA] |  |  |  |
|  |  |  |  |  |  | \*1/\*2 | 98 | Mean 45.4 | Sd 16.1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*3 | 30 | Mean 45.9 | Sd 15.8 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 | 20 | Mean 50.4 | Sd 15.1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*3 | 14 | Mean 53.9 | Sd 15.1 |  |  |  |  |  |  |  |
|  |  |  |  | Max aggregation with 20 μmol/L ADP-Aggmax | 3 days | 1/\*1 | 104 | Mean 53.8 | Sd 15.7 | ANOVA | NR | NR | P=0.003  [across all groups ]  [ANOVA] |  |  |  |
|  |  |  |  |  |  | \*1/\*2 | 98 | Mean 58.1 | Sd 14.7 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*3 | 30 | Mean 59.0 | Sd 15.1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*2 | 20 | Mean 64.1 | Sd 12.1 |  |  |  |  |  |  |  |
|  |  |  |  |  |  | \*2/\*3 | 14 | Mean 67.2 | Sd 11.3 |  |  |  |  |  |  |  |
|  |  | VerifyNow | P2Y12 reaction units (PRU) | 3 days | 1/\*1 | 104 | Mean 231 | Sd 88 | ANOVA | NR | NR | P=0.02  [across all groups ]  [ANOVA] |  |  |  |  |
|  |  |  |  |  | \*1/\*2 | 98 | Mean 245 | Sd 80 |  |  |  |  |  |  |  |  |
|  |  |  |  |  | \*1/\*3 | 30 | Mean261 | Sd 76 |  |  |  |  |  |  |  |  |
|  |  |  |  |  | \*2/\*2 | 20 | Mean 276 | Sd71 |  |  |  |  |  |  |  |  |
|  |  |  |  |  | \*2/\*3 | 14 | Mean 291 | Sd 46 |  |  |  |  |  |  |  |  |
| Jeong, 2012{Jeong, 2012 18322 /id}  22837373  Korea  ACCEL-DM | elective patients LD clopidogrel 300mg.  Acute MI clopidogrel LD 600 mg. after randomization, triple group receive cilostazol 100mg bid, clopidogrel 75mg MD, aspirin 200 mg/d, double group receive clopidogrel 150mg/d MD, and aspirin 200 mg/d. | CYP2C19  in triple treatment group | LTA ADP 20uM maximal PA | LTA ADP 20uM maximal PA | 30-day | \*1/\*1 | 12 | NR | NR | ANOVA | NR | NR | comparing with the lower row 0.647  t-test | NR | NR | NR |
|  |  |  |  |  |  | \*1/LOF | 21 |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | LOF/LOF | 8 |  |  |  |  |  |  |  |  |  |
| Hulot, 2011{Hulot, 2011 18321 /id}  21972404  France  CLOVIS-2 | LD 300 or 900 mg clopidogrel | CYP2C19\*2 | relative  change in platelet aggregation | NR | 6 hrs | \*1/\*1 | 55 | NR | NR | NR | NR | NR | NR | NR | NR | 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 |  |  |  |  |  |  |  |  |  |
| Roberts, 2012{Roberts, 2012 18260 /id}  22464343  Canada  RAPID GENE | CYP2C19\*2 Carriers : 10 mg  prasugrel daily  Non-carriers: 75 mg clopidogrel daily | CYP2C19\*2 | Aggregation by VerifyNow | PRU | 7 days | \*1/\*2 or \*2/\*2 | 46 | 198·8 | Sd 85.6 | T –test | NR | NR | P=0.0011  (carriers vs non carriers) | No | NR |  |
|  |  |  |  |  |  | \*1/\*1 | 141 | 143.8 | Sd 100.5 |  |  |  |  |  |  |  |