**Appendix Table E16. Results from studies assessing the ability of LTA to predict stent thrombosis in patients with ischemic heart disease**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author,year****UID****Country****Study name** | **Treatment** | **Phenotypic Test Used [index test]** | **Clinical Outcome** | **Outcome Definition** | **Timing of measurement** | **Index test result: category (e.g., HPR+) – ONE ROW PER PHENOTYPE GROUP** | **Outcome status (e.g., bleeding or no bleeding)** | **No. with outcome status within phenotype group** | **Comparative metric (OR, RR, HR)** | **95% CI** | **P (between which groups?)****[statistical test]** | **Adjusted?****[YES/NO/NR]****If YES, for what factors?** | **Procedures for multiple comparisons [YES, NO, NR]** | **Comments (e.g., additional data in figures)** |
| Cuisset, 2009{Cuisset, 2009 111 /id}19801028FranceNR | Clopidogrel LD 600 mg | ADP stimulated platelate aggregation | Subacute stent thrombosis  | Subacute stent thrombosis | 30 days | ADG-Ag >67% as non responders N=NR | Subacute stent thrombosis | 31% as nonresponders  | OR=5.8 | 1.9-24.6 | 0.003[logistic regression] | NO | NR |  |
|  | Clopidogrel LD 600 mg | ADP stimulated platelate aggregation | Subacute stent thrombosis  | Subacute stent thrombosis | 30 days | ADG-Ag >67% as non responders N=NR | Subacute stent thrombosis | 31% as nonresponders  | OR=6.24 | 1.6-24.6 | 0.009[logistic regression] | Yes. Age, gender, stent length, left ventricular ejection fraction, diabetes mellitus.  | NR |  |
| Breet,2010{Breet, 2010 86 /id}20179285NetherlandsPOPULAR | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily  | ADP LTA 5µmol/L | Stent thrombosis  | Stent thrombosis  | 1-year  | High OTPRN=445 | Stent thrombosis  | 7 (1.6) | OR=1.59 | 0.53-4.77 | <0.40(high vs normal)[logistic regression] | No  | NR |  |
|  |  |  |  |  |  | Normal OTPRN=604 |  | 6 (1) |  |  |  |  |  |  |
|  | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily | ADP LTA 20 µmol/L | Stent thrombosis  | Stent thrombosis  | 1-year  | High OTPRN=445 | Stent thrombosis  | 9 (2.3) | OR=3.85 | 1.18-12.58 | <0.017(high vs normal)[logistic regression] | No  | NR |  |
|  |  |  |  |  |  | Normal OTPRN=604 |  | 4 (0.6) |  |  |  |  |  |  |
| Kim, 2010{Kim, 2010 241 /id}20449634KoreaNR | 300-600mg LD and 75 mg maintain dose clopidogrel  | 5umol/L ADP LTA | stent thrombosis  | stent thrombosis | 6 months |  <50% | stent thrombosis | 1.2% | OR=2.83 | 1.18-6.80 | 0.015(<50 vs ≥ 50%)[logistic regression] | NR | NR |  |
|  |  |  |  |  |  | ≥50% |  | 3.4% |  |  |  |  |  |  |
| Blindt, 2007{Blindt, 2007 189 /id}18064332 GermanyNR | 75 mg clopidogrel | ADP-LTA | Stent thrombosis  | Stent thrombosis | 6 months | NR | NR | NR | OR=1.059 | 1.00-1.21 | 0.049[logistic regression] | No  | NR |  |
| Gori,2008{Gori, 2008 151 /id}19132241Italy RECLOSE | Clopidogrel+aspirin | LTA-ADP | Stent thrombosis | definite or probable: ACS+either angiographic confirmation of thrombosis or pathological confirmation of thrombosis; or unexplained death or MI in the territory supplied by a stented vessel without angiographic confirmation | 6 mo | RPR (n=90) | YES event | 6 | NR | NR | <0.05 (RPR vs no RPR)[chi square] | NR | NR | NONE |
|  |  |  |  |  |  | No RPR (n=656) |  | 14 | NR | NR |  | NR | NR |  |
|  |  | LTA-collagen |  |  |  | RPR (n=78) |  | 8 | NR | NR | <0.001 (RPR vs no RPR)[chi square] | NR | NR |  |
|  |  |  |  |  |  | No RPR (n=668) |  | 11 | NR | NR |  | NR | NR |  |
|  |  | LTA- ADP+LTA-collagen |  |  |  | RPR (n=32) |  | 6 | NR | NR | <0.001 (RPR vs no RPR)[chi square] | NR | NR |  |
|  |  |  |  |  |  | No RPR (n=714) |  | 14 | NR | NR |  | NR | NR |  |
|  |  | LTA-ADP | Stent thrombosis |  |  | RPR (n=90) |  |  | * AUC 0.65+/-0.06 (cutoff 46%)
* 30% (11-54%)sensitivity
* 88% (86-91%) specificity
 |  | NS |  |  | For this entire section of data: NR what ranges (e.g., “(11-54)” to the left) mean for clinical validity dataAlso ROC curves are in Fig 2Also bootstrap data re cutoff in text |
|  |  | LTA-collagen |  |  |  | RPR (n=78) |  | NA | * AUC 0.50+/-0.07 (cutoff 55%)
* 45% (23-69%) sensitivity
* 90% (88-92%) specificity
 |  | For specificity, “p<0.0001 vs RPR by collagen”  | NR | NR |  |
|  |  | LTA-ADP+LTA-collagen |  |  |  | RPR (n=31) |  |  | * 30% (10-50%) sensitivity
* 97% (95-98%) specificity
 |  | For specificity, <0.01vs. LTA-ADP alone and vs. LTA-collagen |  |  |  |
|  |  | LTA-ADP among patients at high risk for AEs | Stent thrombosis |  |  | RPR (n=352) |  | NA | * 70% (50-90%) sensitivity
* 53% (506-57%) specificity
 |  | For specificity, <0.0001 vs. LTA- collagen | NR | NR |  |
|  |  | LTA-collagen among patients at high risk for AEs |  |  |  | RPR (n=78) |  | NA | * 50% (28-72%) sensitivity
* 91% (88-93%) specificity
 |  | For specificity, p<0.0001 vs. LTA-ADP | NR | NR |  |
|  |  | LTA-ADP+LTA-collagen among patients at high risk for AEs |  |  |  | RPR (n=61) |  | NA | * 45% (23-67%) sensitivity
* 93% (91-95%) specificity
 |  | For specificity, <0.0001 vs. LTA-ADP alone and <0.0001 vs. LTA-collagen alone | NR | NR |  |
|  |  | LTA-ADP | Stent thrombosis |  |  | RPR |  |  | OR 3.28 | 1.23-8.75 | 0.018 Univariate analysis | NR | NR |  |
|  |  | LTA-collagen |  |  |  | RPR |  |  | OR 7.79 | 3.12-19.46 | 0.0001 Univariate analysis | NR | NR |  |
|  |  | LTA-ADP+LTA-collagen |  |  |  | RPR |  |  | OR 12.01 | 4.26-33.87 | 0.0001 Univariate analysis | NR | NR |  |
|  |  | LTA-ADP | Stent thrombosis |  |  | RPR |  | NR | OR 2.41 | 0.99-6.85 | 0.090 (RPR vs no RPR)[Logistic regression] | Clinical characteristics (age, sex, cardiovascular risk factors, ejection fraction, number of vessel disease, renal failure, total stent length, chronic total occlusion, bifurcation lesion and glycoprotein IIb/IIa inhibitors) were included in the logistic regression analysis as independent variables in a model in which each RPR was added separately. | NR |  |
|  |  | LTA-collagen |  |  |  | RPR |  | NR | OR 5.45 | 2.05-14.53 | 0.001 Multivariate analysis | YES | NR |  |
|  |  | LTA-ADP+LTA-collagen |  |  |  | RPR |  | NR | OR 7.50 | 2.40-23.43 | 0.001 Multivariate analysis | Yes  | NR |  |
| Breet, 2011{Breet, 2011 15 /id}21478385The NetherlandsPOPular | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | LTA5 | ST | ST | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPRN=385 | ST | 4 | OR (calculated): 1.1 | 0.3-4.2 | P=1.0 (high + dual vs responders + high aspirin)[fishers exact] | NR | NR |  |
|  | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | LTA20 | ST | ST | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPRN=335 | ST | 5 | OR (calculated): 2.2 | 0.6-8.2 | P=0.3 (high + dual vs responders + high aspirin)[fishers exact] | NR | NR |  |
| Buonamici, 2007{Buonamici, 2007 200 /id}17572245ItalyNR | Clopidogre l LD 600 mg maintenance dose of 75 mg daily  | LTA ADP | Stent thrombosis  | Definite or probable stent thrombosis  | 6 months  | RespondersN=699 | Stent thrombosis |  16 (2.3) | NR | NR | <0.001 (responders vs nonresponders)[chi square] | NR | NR  |  |
|  |  |  |  |  |  | Nonresponders N=105 |  | 9 (8.6) |  |  |  |  |  |  |
|  | Clopidogre l LD 600 mg maintenance dose of 75 mg daily  | LTA ADP | Stent thrombosis  | Stent thrombosis | 6 months  | Responders | Stent thrombosis | 7/699 (3.5) | NR | NR | <0.001 (responders vs nonresponders)[chi square] | NR | NR  |  |
|  |  |  |  |  |  | Non-responders  |  | 4/105(22)  |  |  |  |  |  |  |
|  | Clopidogre l LD 600 mg maintenance dose of 75 mg daily | LTA ADP | Stent thrombosis  | Stent thrombosis | 6 months | Nonresponsiveness  | Stent thrombosis | 105 | HR=3.85 | 1.7-8.71 | <0.001[cox regression] | No  | NR |  |
|  | Clopidogre l LD 600 mg maintenance dose of 75 mg daily  | LTA ADP | Stent thrombosis  | Stent thrombosis | 6 months | Nonresponsiveness  | Stent thrombosis | 105 | HR=3.08 | 1.32-7.16 | 0.009[cox regression] | Yes. Acute myocardial infarction, total stent length, LVEF per 1% increase |  |  |
| Geisler 2010{Geisler, 2010 101 /id}19812059GermanyNR | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | Stent Thrombosis | Academic research consortium(ARC) definition | 3 months | Low responder (Terrtile 3) | Stent Thrombosis | 15 (2%) | NR | NR | p=0.03(low responder vs responder)[KM survival analysis - log rank test] | NO | NR | primary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | 14 (4.6%) |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | Early Stent Thrombosis | Academic research consortium(ARC) definition | 30 days | Low responder (Terrtile 3) | Early Stent Thrombosis | NR | NR | NR | p=0.02(low responder vs responder)[KM survival analysis - log rank test] | NO | NR | primary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | NR |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | Late Stent Thrombosis | Academic research consortium(ARC) definition | 3 months | Low responder (Terrtile 3) | late Stent Thrombosis | NR | NR | NR | p=0.31(low responder vs responder)[KM survival analysis - log rank test] | NO | NR | primary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | NR |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | Stent Thrombosis | Academic research consortium(ARC) definition | 3 months | Low responder (Terrtile 3) | Stent Thrombosis | 15 (2%) | OR=2.31 | 1.1-4.84 | p=0.02(low responder vs responder)[Chi square] | NO | NR | primary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | 14 (4.6%) |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | Definite Stent Thrombosis | Academic research consortium(ARC) definition | 3 months | Low responder (Terrtile 3) | definite Stent Thrombosis | 7 (1%) | OR=1.2 | 0.35-4.13 | p=0.02(low responder vs responder)[Chi square] | NO | NR | primary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | 4 (1.2%) |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | Probable Stent Thrombosis | Academic research consortium(ARC) definition | 3 months | Low responder (Terrtile 3) | Probable Stent Thrombosis | 5 (0.7%) | OR=3.85 | 1.28-11.59 | p=0.01(low responder vs responder)[Chi square] | NO | NR | primary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | 9 (2.7%) |  |  |  |  |  |  |
|  | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | Possible Stent Thrombosis | Academic research consortium(ARC) definition | 3 months | Low responder (Terrtile 3) | Possible Stent Thrombosis | 2 (0.3%) | OR=2.1 | 0.3-15 | p=0.45(low responder vs responder)[Chi square] | NO | NR | primary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | 2 (0.6%) |  |  |  |  |  |  |
| Giusti, 2009{Giusti, 2009 134 /id}19268736ItalyRECLOSE study(Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | Aspirin (loading dose = 325 mg; maintenance dose = 325 mg per day) and clopidogrel (loading dose = 600 mg; 75 mg maintenance). | LTA- ADP | Stent thrombosis | Definite or probable stent thrombosis. Definite = ACS + angiographic or pathologic confirmation of thrombosis; probable = unexplained death or MI in the territory supplied by a stented vessel without angiographic confirmation | Maximum FU of 6 mo | Residual platelet reactivity (RPR) (ADP-induced platelet aggregation ≥70%) | Stent thrombosis present | 8 (7.3%) | NR | NR | 0.001 across groups (chi square test) | NO | NO | Primary outcome |
|  |  |  |  |  |  | No residual platelet reactivity (RPR)  |  | 16 (2.4%)­ |  |  |  |  |  |  |
|  | Aspirin (loading dose = 325 mg; maintenance dose = 325 mg per day) and clopidogrel (loading dose = 600 mg; 75 mg maintenance). | Combination of genotypic and phenotypic tests: CYP2C19\*2 + ADP residual platelet reactivity  | Stent thrombosis | Definite or probable stent thrombosis. Definite = ACS + angiographic or pathologic confirmation of thrombosis; probable = unexplained death or MI in the territory supplied by a stented vessel without angiographic confirmation | Maximum FU of 6 mo | \*2/\*2 + RPRN = 40 | Stent thrombosis present | 6 (15%) | NROR=5.79 | NR(1.04, 39.01) | <0.0001 across groups (chi square test)0.033 (logistic regression) | NOAdjusted (“for traditional cardiovascular risk factors and clinical and procedural risk factors for stent thrombosis”) | NO | Primary outcome |
|  |  |  |  |  |  | \*1/\*1 or low RPRN = 732 |  | 18 (2.5%) |  |  |  |  |  |  |
|  | Aspirin (loading dose = 325 mg; maintenance dose = 325 mg per day) and clopidogrel (loading dose = 600 mg; 75 mg maintenance). | LTA-ADP | Stent thrombosis | Definite or probable stent thrombosis. Definite = ACS + angiographic or pathologic confirmation of thrombosis; probable = unexplained death or MI in the territory supplied by a stented vessel without angiographic confirmation | Maximum FU of 6 mo | Residual platelet reactivity (RPR) (ADP-induced platelet aggregation ≥70%) | Stent thrombosis present | 8 (7.3%) | OR=3.17OR=3.08 | (1.32, 7.59)(1.23, 7.72) | 0.001 (chi square test)0.016 (logistic regression) | NO (univariate)YES (ADP-RPR, traditional cardiovascular risk factors, clinical and procedural risk factors for ST) | NO | Primary outcome |
|  |  |  |  |  |  | No residual platelet reactivity (RPR)  |  | 16 (2.4%) |  |  |  |  |  |  |
| Gori, 2008 {Gori, 2008 164 /id}18718420ItalyRECLOSE study(Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | definite or probable stent thrombosis | definite or probable stent thrombosis | 6 months | Clopidogrel nonresponder | definite or probable stent thrombosis | NR | HR=1.44 | 0.54 to3.82 | P=0.463[Cox regression] | YES;age (years), male gender, family history of CAD, smoker, HTN, hypercholesterolemia, diabetes mellitus, history of myocardial infarction, history of coronary surgery, acute coronary syndrome, acute STEMI, left ventricular ejection fraction (%), multivessel disease, bifurcation lesion, thrombus-containing lesion, chronic total occlusion, and stent length (mm). | NR | Primary endpoint |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | definite or probable stent thrombosis | definite or probable stent thrombosis1 | 6 months | Clopidogrel & Aspirin nonresponder | definite or probable stent thrombosis | NR | HR=3.18 | 1.14 to8.83 | P=0.027[Cox regression] | YES;age (years), male gender, family history of CAD, smoker, HTN, hypercholesterolemia, diabetes mellitus, history of myocardial infarction, history of coronary surgery, acute coronary syndrome, acute STEMI, left ventricular ejection fraction (%), multivessel disease, bifurcation lesion, thrombus-containing lesion, chronic total occlusion, and stent length (mm). | NR | Primary endpoint |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | definite or probable stent thrombosis | definite or probable stent thrombosis**Error! Bookmark not defined.** | 6 months | Clopidogrel non with r without Aspirin responder | definite or probable stent thrombosis | 6 /90 (6.7) | HR=3.15 | 1.21 to8.20 | P=0.019[Cox regression] | NO | NR | Primary endpoint |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | definite or probable stent thrombosis | definite or probable stent thrombosis1 | 6 months | Clopidogrel responder and Aspirin responder | definite or probable stent thrombosis | 12 (2.1) | NR | NR | p<0.0001; (dual clopidogrel and aspirin nonresponders versus aspirin nonresponders)p<0.05(dual clopidogrel and aspirin nonresponders versus aspirin nonresponders) | NO | NR | Primary endpoint |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin nonresponder |  | 5 (11.1) |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin responder  |  | 1 (2.2) |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel responder and aspirin nonresponder |  | 2 (2.3) |  |  |  |  |  |  |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | definite or probable stent thrombosis | definite or probable stent thrombosis1 | 6 months | Clopidogrel responder and Aspirin responder | definite or probable stent thrombosis | NR | NR | NR | p<0.001; (dual nonresponders vs. dual responders)P=0.036(dual nonresponders vs. aspirin nonresponders)P=0.096 (dual nonresponders vs. clopidogrel nonresponders) | NO | NR | Primary endpoint |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | definite stent thrombosis | definite stent thrombosis**Error! Bookmark not defined.** | 6 months | Clopidogrel responder and Aspirin responder | definite stent thrombosis | 6 (1.1) | NR | NR |  | NO | NR | Primary endpoint |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin nonresponder |  | 2 (4.4) |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin responder  |  | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel responder and aspirin nonresponder |  | 1 (1.2) |  |  |  |  |  |  |
|  | 600 mg clopidogrel LD + 75-mg MD & Aspirin 325 mg MD | LTA | probable stent thrombosis | probable stent thrombosis **Error! Bookmark not defined.** | 6 months | Clopidogrel responder and Aspirin responder | probable stent thrombosis | 6 (1.1) | NR | NR | p <0.05 (dual clopidogrel and aspirin nonresponders versus clopidogrel and aspirin responders) | NO | NR | Primary endpoint |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin nonresponder |  | 3 (6.7) |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel nonresponder and aspirin responder  |  | 1 (2.2) |  |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel responder and aspirin nonresponder |  | 1 (1.2) |  |  |  |  |  |  |
| Gurbel, 2008{Gurbel, 2008 157 /id}19012177USANone | Clopidogrel+aspirin | 5 uM ADP aggregation | Stent thrombosis |  | 1 mo | >46% platelet aggregation (HPR) |  | 1 | NR | OR (calculated): 3.7 | 0.6-22.3 | P=0.16 (HPR vs NPR)[fishers exact] | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 1 mo | <=46% |  | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 0 | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 20 uM ADP aggregation | Stent thrombosis |  | 1 mo | >64.5% platelet aggregation (HPR) |  | 1 | NR | OR (calculated): 3 | 0.5-18.1 | P=0.34 (HPR vs NPR)[fishers exact] | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 1 mo | <=46% |  | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 0 | NR | NR | NR | NR | NR | NR |
| Liu, 2011{Liu, 2011 12 /id}21613806ChinaNone | Clopidogrel+aspirin | Aggregometry | Stent thrombosis |  |  | Nonrespoders | 34 | 0 |  | OR (calculated): 16 | 0.8-321.2 | P=0.03 (HPR vs NPR)[fishers exact] |  |  |
|  |  |  |  |  |  | Low responders | 28 | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responders | 44 | 0 |  |  | NR |  |  |  |
|  | Clopidogrel+aspirin | Aggregometry | Stent thrombosis |  |  | Nonrespoders | 34 | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Low responders | 28 | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responders | 44 | 0 |  |  | NR |  |  |  |
| Muller, 2003{Muller, 2003 223 /id}12719773GermanyNone | Clopidogrel+aspirin | Aggregometry | Subactute stent thrombosis | Day 6 or 7 after angiography | Day 6 or 7 | Nonresponder (NB authors don’t say according to which level of ADP or both) | Yes event | 2 | OR (calculated): 143 | 5.7-3586 | P=0.001 (nonresp vs others)[fishers exact] | NR | NR | NONE |
|  |  |  |  |  |  | Semiresponder |  | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responder |  | 0 |  |  |  |  |  |  |
| Muller, 2010{Muller, 2010 51 /id}20728084GermanyNR | Clopidogrel 600 mg LD + 75 mg MD & Aspirin 100 mg/d MD | LTA | Stent thrombosis | Defined according to the Academic Research Consortium criteria | Mean follow up of 344 days | Stratum I: RPA & CRP <median | Stent thrombosis | NR | NR | NR | P=0.02(Stratum IV vs I)P<0.001(Stratum IV vs II)P=0.04(Stratum IV vs III)P>0.05 (Stratum III vs I+II)P>0.05(Stratum II vs I)[Log Rank ]test | YES;age,gender, left ventricular function, acute coronary syndromes, hyperlipidemiaand relevant comedication | NR | Primary |
|  |  |  |  |  |  | Stratum II:RPA >median & CRP ≤median |  | NR |  |  |  |  |  |  |
|  |  |  |  |  |  | Stratum III:RPA ≤ median & CRP >median |  | NR |  |  |  |  |  |  |
|  |  |  |  |  |  | Stratum IV:RPA & CRP >median |  | NR |  |  |  |  |  |  |
| Trenk, 2008{Trenk, 2008 171 /id}18482659GermanyEXCELSIOR (Impact of Extent of Clopidogrel- Induced Platelet Inhibition During Elective Stent Implantationon Clinical Event Rate) | 600 mg clopidogrel LD + 75 mg/day MD (for 30 d w/ bare-metal stents or 6 mth w/ atleast 1 drug-eluting stent | LTA | Any stent thrombosis | Any stent thrombosis | 1 year | high on-treatment plateletreactivity (RPA>14%) N=217 | Any stent thrombosis | 10(4.6%) | HR=3.7 | 1.4-9.6 | P=0.008 (between high and not high residual platelet reactivity)[Cox regression] | YES;Age, HTN, DM, BMI, platelet count, verapamil, insulin and antidiabetic medication use, previous angioplasty and CABG, LV function, angina class, PCI, stent implantation, LAD affected, stenosis length ad diameter of stenosis  | NR | Primary outcome |
|  |  |  |  |  |  | no high on-treatment plateletreactivity (RPA≤ 14%)N=548 |  | 7 (1.3%) |  |  |  |  |  |  |
|  | 600 mg clopidogrel LD + 75 mg/day MD (for 30 d w/ bare-metal stents or 6 mth w/ atleast 1 drug-eluting stent | LTA | Definite or probable stent thrombosis | Definite or probable stent thrombosis | 1 year | high on-treatment plateletreactivity (RPA>14%) N=217 | Definite or probable stent thrombosis | 8 (3.7%) | HR=4.1 | 1.3-12.5 | P=0.01 (between high and not high residual platelet reactivity)[Cox regression] | YES;Age, HTN, DM, BMI, platelet count, verapamil, insulin and antidiabetic medication use, previous angioplasty and CABG, LV function, angina class, PCI, stent implantation, LAD affected, stenosis length ad diameter of stenosis  | NR | Primary outcome |
|  |  |  |  |  |  | no high on-treatment plateletreactivity (RPA≤ 14%)N=548 |  | 5 (0.9%) |  |  |  |  |  |  |
|  | 600 mg clopidogrel LD + 75 mg/day MD (for 30 d w/ bare-metal stents or 6 mth w/ atleast 1 drug-eluting stent | LTA | Definite stent thrombosis | Definite stent thrombosis | 1 year | high on-treatment plateletreactivity (RPA>14%) N=217 | Definite stent thrombosis | 1(0.5%) | HR=1.3 | 0.1-14.1 | P=0.84 (between high and not high residual platelet reactivity)[cox regression] | YES;Age, HTN, DM, BMI, platelet count, verapamil, insulin and antidiabetic medication use, previous angioplasty and CABG, LV function, angina class, PCI, stent implantation, LAD affected, stenosis length ad diameter of stenosis  | NR | Primary outcome |
|  |  |  |  |  |  | no high on-treatment plateletreactivity (RPA≤ 14%)N=548 |  | 2 (0.4%) |  |  |  |  |  |  |
|  | 600 mg clopidogrel LD + 75 mg/day MD (for 30 d w/ bare-metal stents or 6 mth w/ atleast 1 drug-eluting stent | LTA | Probable stent thrombosis | Probable stent thrombosis | 1 year | high on-treatment plateletreactivity (RPA>14%) N=217 | Probable stent thrombosis | 7 (3.2%) | HR=5.9 | 1.5-23 | P=0.01 (between high and not high residual platelet reactivity)[cox regression] | YES;Age, HTN, DM, BMI, platelet count, verapamil, insulin and antidiabetic medication use, previous angioplasty and CABG, LV function, angina class, PCI, stent implantation, LAD affected, stenosis length ad diameter of stenosis  | NR | Primary outcome |
|  |  |  |  |  |  | no high on-treatment plateletreactivity (RPA≤ 14%)N=548 |  | 3 (0.5%) |  |  |  |  |  |  |
|  | 600 mg clopidogrel LD + 75 mg/day MD (for 30 d w/ bare-metal stents or 6 mth w/ atleast 1 drug-eluting stent | LTA | Possible stent thrombosis | Possible stent thrombosis | 1 year | high on-treatment plateletreactivity (RPA>14%) N=217 | Possible stent thrombosis | 2(0.9%) | HR=2.6 | 0.4-18.4 | P=0.34 (between high and not high residual platelet reactivity)[cox regression] | YES;Age, HTN, DM, BMI, platelet count, verapamil, insulin and antidiabetic medication use, previous angioplasty and CABG, LV function, angina class, PCI, stent implantation, LAD affected, stenosis length ad diameter of stenosis  | NR | Primary outcome |
|  |  |  |  |  |  | no high on-treatment plateletreactivity (RPA≤ 14%)N=548 |  | 2(0.4%) |  |  |  |  |  |  |
| Wang, 2010{Wang, 2010 37 /id}21171668ChinaNone | Clopidogrel+aspirin | LTA | Definite or probable stent thrombosis | Academic Research Consortium (ARC) definitions: Definite—presence of ACS with angiographic or autopsy evidence of thrombus or occlusionProbable --unexplained deaths within 1 month after the procedure or acute MI involving target-vessel territory without angiographic confirmation |  | Clopidogrel resistance |  | 4 (12.5%) | OR=8.6 | 1.49-49.15 | 0.017 (resisters vs nonresistant)(Student’s t); p=0.025 from multivariate regression (for indpendent prediction) | YES for multivariate regression P value only (diabetes, BMI, and smoking status) |  |  |
|  |  |  |  |  |  | nonresistance |  | 2 (1.64%) |  |  |  |  |  |  |
|  | Clopidogrel+aspirin | LTA | Definite |  |  | Clopidogrel resistance |  | 2 (6.25%) | OR=8.1 | 0.71-91.95 | 0.110 (resisters vs nonresistant) (Student’s t) | NR |  |  |
|  |  |  |  |  |  | nonresistance |  | 1 (0.82%) |  |  |  |  |  |  |
|  | Clopidogrel+aspirin | LTA | Probable |  |  | Clopidogrel resistance |  | 2 (6.25%) | OR=8.1(calculate) | 0.71-91.95 | 0.110 (resisters vs nonresistant) (Student’s t) | NR |  |  |
|  |  |  |  |  |  | nonresistance |  | 1 (0.82%) |  |  |  |  |  |  |
|  | Clopidogrel+aspirin | LTA | Acute | within 24 hours |  | Clopidogrel resistance |  | 0 | OR=3.76 (calculated) |  | NR | NR |  |  |
|  |  |  |  |  |  | nonresistance |  | 0 |  |  |  |  |  |  |
|  | Clopidogrel+aspirin | LTA | Subacute | 1–30 days after |  | Clopidogrel resistance |  | 1 (3.13%) | OR=3.90 (calculated) | 0.24-64.17 | 0.373 (resisters vs nonresistant) (Student’s t) | NR |  |  |
|  |  |  |  |  |  | nonresistance |  | 1 (0.82%) |  |  |  |  |  |  |
|  | Clopidogrel+aspirin | LTA | Late | 30 days to 1 year after |  | Clopidogrel resistance |  | 3 (9.38%) | OR=12.52 (calculated) | 1.26-124.75 | 0.028 (resisters vs nonresistant) (Student’s t) | NR |  |  |
|  |  |  |  |  |  | nonresistance |  | 1 (0.82%) |  |  |  |  |  |  |
| Wang, 2009{Wang, 2009 130 /id}19041120ChinaNR | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | Definite or probable stent thrombosis  | Definite or probable stent thrombosis | 12-months | Clopidogrel resistance  | Definite or probable stent thrombosis | NR | HR=4.46 | 1.03-20.27 | 0.031[cox regression] | Yes, LV dysfunction (EF<30%),Total stent length | NR |  |
|  | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | Definite or probable stent thrombosis | Definite or probable stent thrombosis | One year  | Clopidogrel resistance N=65 | Definite or probable stent thrombosis | 6 (9.2) | NR | NR | 0.018 (resisters vs normal response) | NO | NO  |  |
|  |  |  |  |  |  | Normal response N=321 |  | 8(2.5) |  |  |  |  |  |  |
|  | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | Definite stent thrombosis | Definite stent thrombosis | One year  | Clopidogrel resistance N=65 | Definite stent thrombosis | 3 (4.6) | OR=3.8 ( calculate) | 0.84-17.56 | 0.096 (resisters vs normal response) | NO | NO  |  |
|  |  |  |  |  |  | Normal response N=321 |  | 4(1.2) |  |  |  |  |  |  |
|  | LD 300 mg clopidogrel and maintaining 75 mg daily  | ADP-LTA | Probable stent thrombosis | Probable stent thrombosis | One year  | Clopidogrel resistance N=65 | Probable stent thrombosis | 3 (4.6) | OR=3.83 | 0.84-17.56 | 0.096 (resisters vs normal response) | NO | NO  |  |
|  |  |  |  |  |  | Normal response N=321 |  | 4 (1.2) |  |  |  |  |  |  |
| Gurbel, 2003{Gurbel, 2003 222 /id}12796140USANR | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | Stent thrombosis | Stent thrombosis | 30 days | Clopidogrel resistance | Stent thrombosis | 0/50 | OR (calculated): 1.3 | NR | P=0.9 (nonresp vs others)[fishers exact] | NO | NO  |  |
|  |  |  |  |  |  | Clopidogrel nonresistance |  | 0/63 |  |  |  |  |  |  |
| Gaglia, 2012{Gaglia, 2011 18244 /id}21919956USANR | LD: 600 mg loading clopidogrel or 75-mg for 5 days MD: Aspirin + clopidogrel 75 mg for 1 month in patients with BMS and 12 months in patients receiving DES | LTA 5 µmol/L ADP | stent thrombosis | stent thrombosis | 3 days | HPR with 5 μM ADP MPA >46% : n=46 | HPR | 0 | OR (calculated)=3.3 | NR | 0.6(HPR vs NPR)[Fishers exact test] | No | NR |  |
|  |  |  |  |  |  | NPR with 5 μM ADP MPA >46% : n=154 |  | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | HPR with 20 μM ADPMPA >60% n=32 | HPR | 0 | OR (calculated)=5.2 | NR | 0.4(HPR vs NPR)[Fishers exact test] | No | NR |  |
|  |  |  |  |  |  | NPR with 20 μM ADPMPA >60% n=168 |  | 0 |  |  |  |  |  |  |