**Appendix Table E11. Phenotypic test details in studies assessing the predictive ability of LTA in patients with ischemic heart disease**

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| --- | --- | --- | --- | --- | --- | --- |
| **Author, year [ref]**  **UID**  **Country**  **Study Name** | **Test/Device name**  **Device category Device name & manufacturer\*** | **Agonist used** | **Sample Collection and Procurement**  **Anticoagulant used**  **Interval between clopidogrel doses and blood sampling (in days)**  **Interval between sampling and testing (in days):** | **Grouping of Phenotypes [Definition]** | **Rational for the grouping of phenotypes reported (Yes/No)**  **[short description]** | **Frequency of phenotypes** |
| Angiolollo, 2007{Angiolillo, 2007 194 /id}  17936152  Spain  NR | Light transmittance aggregometry  ChronoLog 490  Model  ChronoLog Corp., Havertown, Pennsylvania | ADP | Blood samples for platelet function assays were collected 2 to 4 h after antiplatelet therapy intake  NR  2 to 4 h after antiplatelet therapy intake.  NR | HRP (set a cutoff of 62% Aggmax )  non HRP | Based on ROC curve | HRP (set a cutoff of 62% Aggmax.): n=45(26)  non HRP: n=128 (73) |
| Aradi, 2008{Aradi, 2008 236 /id}  18388039  Hungary  NR | Optical aggregometry  Carat TX4 optical aggregometer  Carat Diagnostics, Budapest, Hungary | adenosine diphosphate 5 and 10 umol, collagen 2 ug/ml, and adrenaline 10 umol | 10 mL blood was drawn by direct venipunc ture for optical aggregometry into a sodium citrate vacuum tube  Sodium citrate  Clopidogrel given at time of PCI and stenting and platelets tested at 30 ± 5 days after coronary stent implantation  2 hours | Lower 50% of ADP 5 umol Induced Aggregation  Upper 50% of ADP 5 umol Induced Aggregation | Not explicitly reported | Lower 50% of ADP 5 umol Induced Aggregation: NR but maybe can ascertain from Fig 1A (distribution of aggregation %s)  Upper 50% of ADP 5 umol Induced Aggregation: NR but maybe can ascertain from Fig 1A (distribution of aggregation %s) |
| Bellemain-Appaix, 2010{Bellemain-Appaix, 2010 87 /id}  20170822  France  ALBION (Assessment of the Best Loading Dose of Clopidogrel to Blunt Platelet Activation, Inflammation and Ongoing Necrosis) | LTA  NR  NR | 20 µmol/l ADP | Samples obtained at baseline and 0.5, 1, 2, 3, 4, 5, 6, and 24 h  NR  Less than 1 day; Clopidogrel came first  NR | Slow responders (maximal platelet aggregation <10% within the first hour after loading)  Fast responders (maximal platelet aggregation ≥10% within the first hour after loading)  Low response (maximal platelet aggregation <10% over 24 hrs)  Responders (maximal platelet aggregation ≥10% over 24 hrs) | Not explicitly reported | Slow responders (maximal platelet aggregation <10% within the first hour after loading): 53 (55%)  Fast responders (maximal platelet aggregation ≥10% within the first hour after loading): 46 (45%)    Low response (maximal platelet aggregation <10% over 24 hrs): 9 (9.3%)  Responders (maximal platelet aggregation ≥10% over 24 hrs) : 7 (90.7%) |
| Bliden,  2007{Bliden, 2007 202 /id}  17291930  USA  NR | Platelet aggregation/Chronolog Lumi-Aggregometer  Model 490-4D  Chronolog, Havertown, Pennsylvania | 5 umol/LADP and 1 mmol/Larachidonic acid (AA) | from patients in a fasting state in the catheterization laboratory through the indwelling femoral vessel sheath.  3.8% trisodium citrate or lithium heparin  Baseline samples were obtained before coronary intervention and at 3 h and 18 to 24 h after stenting  Within 2h | HPR=high on-treatment platelet reactivity based on LTA-5 umol/L ADP (%) | Based on literature | HPR=high on-treatment platelet reactivity based on LTA-5 umol/L ADP (%) : 22%Gori |
| Blindt, 2007{Blindt, 2007 189 /id}  18064332  Germany  NR | Platelet aggregation /Densitometrically-determined measurement of platelet aggregation  APACT 4 S  Plus platelet aggregometer  Rolf Greiner Biochemica, Flacht,  Germany | 10 µM ADP | The blood samples were obtained  72–96 h after stent placement. Interval at least 8 days  3.2% citrate  All patients were given 75 mg clopidogrel and 100 mg aspirin once a day at least five days prior to PCI. The blood samples were obtained 72–96 h after stent placement. Interval at least 8 days  Within 1 h | NR | NR | NR |
| Breet, 2010{Breet, 2010 50 /id}  20695984  Netherlands  Substudy of a larger cohort (Breet 2010 PMID: 20179285) | LTA  four-channel APACT 4004  aggregometer  LABiTec, Arensburg, Germany | NR | NR  3.2% citrate  NR  2h | High on-treatment platelet reactivity with native platelet rich plasma  Non-high on-treatment platelet reactivity with native platelet rich plasma (Cutoffs NR)  High on-treatment platelet reactivity with adjusted platelet rich plasma (Cutoffs NR)  Non-high on-treatment platelet reactivity with adjusted platelet rich plasma (Cutoffs NR) | Not explicitly reported | High on-treatment platelet reactivity with native platelet rich plasma (Cutoffs NR) : 200 (28.9%)  Non-high on-treatment platelet reactivity with native platelet rich plasma (Cutoffs NR): 492 (71.1%)    High on-treatment platelet reactivity with adjusted platelet rich plasma (Cutoffs NR): 243 (35.1%)  Non-high on-treatment platelet reactivity with adjusted platelet rich plasma (Cutoffs NR): 449 (64.9%) |
| Breet, 2010{Breet, 2010 86 /id}  20179285  Netherlands  POPULAR | Light transmittance aggregometry  NR  NR | 5 µmol/L ADP  20 µmol/L ADP | Before Heparinization  3.2% citrate  NR  Within 2 hours after blood collection. | High on-treatment platelet reactivity ≥42.9% aggregation LTA-ADP 5 µmol/L N=445  Not High on-treatment platelet reactivity <42.9% aggregation LTA-ADP 5 µmol/L N=604  High on-treatment platelet reactivity <64.5% aggregation LTA-ADP 20 µmol/L n=659  Not high on-treatment platelet reactivity ≥64.5% aggregation LTA-ADP 20 µmol/L n=392 | Based on ROC curves | High on-treatment platelet reactivity ≥42.9% aggregation LTA-ADP 5 µmol/L: N=445  Not High on-treatment platelet reactivity <42.9% aggregation LTA-ADP 5 µmol/L: N=604  High on-treatment platelet reactivity ≥64.5% aggregation LTA-ADP 20 µmol/L: n=392  Not high on-treatment platelet reactivity <64.5% aggregation LTA-ADP 20 µmol/L: n=659 |
| Breet, 2011{Breet, 2011 15 /id}  21478385  The Netherlands  POPular | Light transmission aggregometry  Four-channel APACT 4004 aggregometer  LABiTec, Arensburg, Germany | ADP | NR  3.2% Sarstedt citrate  NR  2h | No HCPR (LTA5)  With HCPR (LTA5)  No HCPR (LTA20)  With HCPR (LTA20)  Cutoff 43% aggregation for LTA5, 65% for LTA20 | Based on literature | No HCPR (LTA5): 536  With HCPR (LTA5): 385  No HCPR (LTA20): 588  With HCPR (LTA20): 335 |
| Buonamici, 2007{Buonamici, 2007 200 /id}  17572245  Italy  NR | LTA  APACT 4 light transmittance aggregometer  Helena Laboratories,  Milan, Italy | ADP | Blood samples anticoagulated with 0.129 mol/l sodium citrate (ratio 9:1) for platelet reactivity assessment was obtained 12 to 18 h from clopidogrel loading  0.129 mol/l sodium citrate  12-18 h from clopidogrel loading  NR | Responders  Non-responders  Patients with platelet aggregation by 10-mol ADP ≥90th percentile of controls (70%) were defined as nonresponders. | Not explicitly reported | Responders : 699/804(86.9)  Non-responders: 105/804 (13.1) |
| Campo, 2007{Campo, 2007 197 /id}  17868803  Italy  NR | Platelet aggregation  NR  NR | ADP | NR  NR  T0 baseline before thienopyridine;  T1, 5-7 days after baseline;  T2, 7-10 days after T1  NR | Responder to both thienopyridines  Clopidogrel nonresponders  Ticlopidine nonresponders Nonresponder to both thienopyridines  [Based on thienopyridine responsiveness] | Not explicitly reported | Responder to both thienopyridines: 90  Clopidogrel nonresponders: 30  Ticlopidine nonresponders: 28  Nonresponder to both thienopyridines: 5 |
| Cuisset, 2006{Cuisset, 2006 212 /id}  16371119  France  NR | light transmittance  PAP4 Aggregometer  Biodata Corp, Wellcome, Paris, France | ADP 10 umol/L | ﬁrst blood millimeters discarded to avoid platelet activation induced by needle puncture and blood was immediately collected in vacutainer tube, ﬁlled to capacity, and then inverted three to ﬁve times for gentle mixing  3.8% Trisodium citrate  before the PCI at least 12 h after the loading dose of clopidogrel and the aspirin administration and before administration of tiroﬁban if needed  Immediately | Quartiles of (mean ± SD) ADP-induced maximal intensity of platelet aggregation (with threshold for low response ≥70%)  Q1, Q2, and Q3: responsive to clopidogrel  Q4 (82 ± 1 2%): nonresponsive to clopidogrel | The quartile data—Q4 range determined the cutoff | Q1, Q2, and Q3: responsive to clopidogrel: 83  Q4 (82 ± 1 2%): nonresponsive to clopidogrel: 23 |
| Cuisset, 2006{Cuisset, 2006 237 /id}  17010792  France  NR | Light transmission  PAP4 Aggregometer  Biodata Corporation, Wellcome, Paris, France | 10 µmol/L ADP | Before PCI after clopidogrel LD  3.8% trisodium citrate  0.5 days (12 hours)Clopidogrel came first  NR | high post treatment platelet reactivity (ADP induced platelet aggregation >70%) in 300 mg group  normal post treatment platelet reactivity (ADP induced platelet aggregation <70%) in 300 mg group    high post treatment platelet reactivity (ADP induced platelet aggregation >70%) in 600 mg group  normal post treatment platelet reactivity (ADP induced platelet aggregation <70%) in 600 mg group | Not explicitly reported | high post treatment platelet reactivity (ADP induced platelet aggregation >70%) in 300 mg group: 36 (24.7%)  normal post treatment platelet reactivity (ADP induced platelet aggregation <70%) in 300 mg group: 110 (75.3%)    high post treatment platelet reactivity (ADP induced platelet aggregation >70%) in 600 mg group: 22 (15.1%)  normal post treatment platelet reactivity (ADP induced platelet aggregation <70%) in 600 mg group: 124 (84.9%) |
| Cuisset, 2007{Cuisset, 2007 204 /id}  17264958  France  NR | Light transmission  PAP4 Aggregometer  Biodata Corporation, Wellcome, Paris, France | ADP | Blood samples for testing platelet reactivity were drawn in the catheterization laboratory from a 6-French arterial sheath before  the PCI  3.8% trisodium citrate  Blood samples were drawn before the PCI, at least 12 h after the loading dose of clopidogrel and aspirin, and before administration of tirofiban if needed  NR | HPPR ADP10 >70  No HPPR ADP10 <70  [Based on high post-treatment platelet reactivity (HPPR) defined as >70% by ADP LTA] | Based on literature | HPPR ADP10 >70: 42 (22)  No HPPR ADP10 <70: 148 (78) |
| Cuisset, 2009{Cuisset, 2009 111 /id}  19801028  France  NR | light transmission aggregometry  PAP4 aggregometer  Bio data welcome, Paris France | 10 umol/L  ADP | blood samples were obtained 72–96 h after stent placement  Citrate  Interval at least 8 days.  NR | Non-responder: ADP-Ag of >67%  Responder: ADP-Ag of ≤67% | As per the ROC curve created using data from study subjects | Non-responder: ADP-Ag of >67%: 31%  Responder: ADP-Ag of ≤67%: 69% |
| Cuisset, 2009{Cuisset, 2009 246 /id}  19736156  France  NR | Light transmission aggregometry  PAP4 Aggregometer  Biodata Corporation, Wellcome, Paris, Francea | ADP | Blood drawn after cardiac catheterization  NR  0.5 days (12 hours after the loading dose of clopidogrel and aspirin)  NR | Hyper-responder (quartile 1: ADP-induced aggregation <40%)  Non hyperresponder (quartile 2-4: ADP-induced aggregation ≥40%) | Not explicitly reported | Hyper-responder (quartile 1: ADP-induced aggregation <40%): 150 (25.1%)  Non hyperresponder (quartile 2-4: ADP-induced aggregation ≥40%): 447 (74.9) |
| Frere, 2007{Frere, 2007 193 /id}  17938809  France  NR | light transmission aggregometry  PAP4 aggregometer  Bio data welcome, Paris France | ADP | before the PCI at least 12 h after the loading dose of clopidogrel and aspirin, and before administration of tirofiban if needed.  3.8% trisodium citrate  After 12hours after the loading dose of clopidogrel  With 1 hour | ADP-Ag ≥ 70%  ADP-Ag <70% | As per the ROC curve created using data from study subjects | ADP-Ag ≥ 70%: 11/14 (79%)  ADP-Ag <70%: 3/14 (21%) |
| Geisler 2008{Geisler, 2008 184 /id}  17949474  Germany  NR | Turbidoaggregometry  Chronolog Lumi aggregometer with Aggro-link software  NR | 20 umol ADP | Venous blood. RPA measured 5 min after ADP addition  3.8% citrate  At least 6 hr after loading dose (median, 24.8 hr) if 600 mg; if 300 mg (for those previously on clopidogrel), at least 24 hr after loading dose  NR | RPA tertile 1 (lowest)  RPA tertile 2  RPA tertile 3 (highest) | Not explicitly reported | RPA tertile 1 (lowest) NR  RPA tertile 2 NR  RPA tertile 3 (highest) NR |
| Geisler 2010{Geisler, 2010 54 /id}  20526607  Germany  NR | Turbidometry;  Chronolog Lumi Aggregometer  Chronolog | ADP (20 umol/l) | NR  Samples were collected the day following PCI  blood was collected at least 6 h (median 23.6 h interquartile range 20.8 h) after first administration of 600 mg clopidogrel  NR | Diabetics with ADP-induced aggregation in the top tertile vs. lowest tertile (among n=413 patients followed) | Prestudy data by the authors in a smaller, different patient group (data reported in current paper but not extracted) | NR |
| Geisler, 2006{Geisler, 2006 210 /id}  17005534  Germany  NR | NR  Chronolog Lumi aggregometer with Aggro-Link  Software  NR | ADP | Blood samples were collected in 3.8%  citrate plasma  3.8% citrate plasma  Patient blood was collected at least 6 h (mean 34.8+25.9 h) after first administration of 600 mg clopidogrel  NR | Adequate response (<70%)  Low response (>70%)  Based on post-treatment aggregation | Based on literature | Adequate response (<70%): 341/363( 93.9)  Low response (>70%): 22/363 (6.1) |
| Geisler, 2010{Geisler, 2010 101 /id}  19812059  Germany  NR | light transmission aggregometry  Chronolog Lumi aggregometer  NR | ADP | 6 hrs after clopidogrel dose  3.8% citrate  0.25 days (6 hours); Clopidogrel came first  NR | Clopidogrel low responders (tertile 3)  Clopidogrel responders (tertile 1 & 2) | Not explicitly reported | Clopidogrel low responders (tertile 3): 329 (32.3%)  Clopidogrel responders (tertile 1 & 2): 690 (67.7%) |
| Giusti, 2009{Giusti, 2009 134 /id}  19268736  Italy  RECLOSE study  (Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | Turbidimetric aggregometry  APACT4 (4 channel aggregometer)  Helena Laboratories (Milan, Italy) | ADP (10 μM) | Venous blood was obtained  Citrated blood  Venous blood was obtained 12-18 h from clopidogrel loading; for patients administered IIb/IIIa inhibitors blood was obtained 6 d after catheterization  NR | Residual platelet reactivity (RPR) (ADP-induced platelet aggregation ≥70%)  No residual platelet reactivity (RPR) | Based on literature | Residual platelet reactivity (RPR) (ADP-induced platelet aggregation ≥70%): 110 (14.2%)  No residual platelet reactivity (RPR): 662 (85.8%) |
| Gori,  2008{Gori, 2008 151 /id}  19132241  Italy  RECLOSE | LTA/NR  APACT 4 light transmittance aggregometer  Helena Laboratories, Milan, Italy | 10 umol ADP or 2 μg/ml collagen | NR  0.109 M sodium citrate  Platelet reactivity measured 12 to 18 hr after clopidogrel loading For patients receiving in the catheterization laboratory both the loading dose of clopidogrel and a IIb/IIIa inhibitor, blood samples were obtained after six days while the patient was on the 75-mg maintenance dose of clopidogrel  NR | All patients  RPR ≥70% by LTA with ADP  No RPR  RPR by LTA with collagen >90th percentile of patients’ distribution  No RPR  RPR by LTA with ADP+LTA with collagen [NB Fig. 1 says n=32 but Table 3 says n=31)  No RPR | LTA-ADP cutoff: Based on literature  LTA-collagen cutoff: NR | All patients  RPR ≥70% by LTA with ADP: 90/746 (12%)  No RPR: 656/746 (88%)  RPR by LTA with collagen >90th percentile of patients’ distribution (56%): 78/746 (10%)  No RPR: 668/746 (90%)  RPR by LTA with ADP+LTA with collagen: 32/746 (4%) [NB Fig. 1 says n=32 but Table 3 says n=31)  No RPR: 714/746 (96%) |
| Gori, 2008 {Gori, 2008 164 /id}  18718420  Italy  RECLOSE study  (Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | light transmission aggregometry  APACT4  Helena  Laboratories, Milan, Italy | 10-μM ADP (clopidogrel) , 1-mM arachidonic acid (aspirin), and 2-μg/ml collagen (clopidogrel) | In catheterization laboratory  0.129 mol/l sodium citrate  0.5-0.75 day (12 to 18 h ); 6 days for those pm glycoprotein (GP) IIb/IIIa inhibitor  clopidogrel came first  NR | Clopidogrel responder (platelet aggregation by ADP <70%; by collagen was defined as platelet aggregation l below 90th percentile of aggregation value distribution that resulted in 56%) and Aspirin responder (platelet aggregation by arachidonic acid ≥20%)  Clopidogrel nonresponder (platelet aggregation by ADP ≥70%; by collagen was defined as platelet aggregation above the 90th percentile of aggregation value distribution that resulted in 56%) and aspirin nonresponsiveness (platelet aggregation by arachidonic acid ≥20%)  Clopidogrel nonresponder (platelet aggregation by ADP ≥70%; by collagen was defined as platelet aggregation above the 90th percentile of aggregation value distribution that resulted in 56%) and aspirin responder (platelet aggregation by arachidonic acid ≥20%)  Clopidogrel responder (platelet aggregation by ADP ≥70%; by collagen was defined as platelet aggregation above the 90th percentile of aggregation value distribution that resulted in 56%) and aspirin nonresponder (platelet aggregation by arachidonic acid ≥20%) | Based on literature | Clopidogrel responder and Aspirin responder : 570 (76.4%)  Clopidogrel nonresponder and aspirin nonresponder: 45 (6%)  Clopidogrel nonresponder and aspirin responder : 45 (6%)  Clopidogrel responder and aspirin nonresponder : 86 (11.6%) |
| Gurbel,  2010{Gurbel, 2010 68 /id}  20691842  USA  PREPARE POST-STENTING | light transmission aggregometry  LumiAggregometer Model 490-4D  Chronolog,  Havertown, PA | 5 μmol/  L ADP  (2 mmol/L arachidonic acid (AA) was also used) | Blood; 18 to 24 hours post-PCI or  5 days post-PCI (if eptifibatide used)  3.2% trisodium citrate  NR; Clopidogrel came first  NR | Quartile of LTA with ADP  Quartile 1 <25 %  Quartile 2 25-35 %  Quartile 3 >35-45 %  Quartile 4 >45 % | Quartiles: Not explicitly reported  Also by ROC analysis within the same cohort | Quartile of LTA with ADP  Quartile 1 <25 %: 56 (25%)  Quartile 2 25-35 %: 56 (25%)  Quartile 3 >35-45 %: 56 (25%)  Quartile 4 >45 %: 57 (25%) |
| Gurbel, 2003{Gurbel, 2003 222 /id}  12796140  USA  NR | LTA  Chronology Lumi-Aggregometer (Model 490-4D)  Chronology, Havertown, Pennsylvania | 5 μm ADP | Response assessed at day 5  3.8% trisodium citrate  2 hours  NR | Drug resistance= <10% difference between baseline aggregation and posttreatment aggregation with 5 μmol/L ADP used as the agonist | Based on literature | Resistance  Nonresistance |
| Gurbel, 2003{Gurbel, 2003 224 /id}  12714161  USA  NR | Platelet aggregation  NR  NR  &  P-selectin expression by flow cytometry  NR  Parmingen, San Diego, California | ADP 5 and 20 umol/liter for LTA & ADP 200 umol/liter for Flow cytometry | Blood was collected in vacutainer tubes  3.8% trisodium citrate  Blood was collected immediately before clopidogrel administration (baseline), and at 1, 5, and 30 days after stenting.  NR | Nonresponder (change from baseline of <10%)  Responder (change from baseline of <10%) | Not explicitly reported | Nonresponder (change from baseline of <10%)  Aggregation by ADP 5 umol/liter: 23/63 (37%)  Aggregation by ADP 20 umol/liter: 13/38 (34%)  Responder (change from baseline of <10%)  Aggregation by ADP 5 umol/liter: 40/63 (63%)  Aggregation by ADP 20 umol/liter: 25/38 (66%) |
| Gurbel, 2004{Gurbel, 2004 220 /id}  15154601  USA  None | aggregometry  Chronolog Lumi-Aggregometer (model 4902D) with AggroLink software  Chronolog, Hawerton [sic], PA | 5 and 20 uM ADP | Blood was collected in vacutainer tubes filled to capacity, and then gently inverted 3–5 times for mixing  3.8% trisodium citrate  obtained before clopidogrel administration and stenting (baseline); and at 2 h, 24 h, 5 days and 30 days post-stenting  NR | heightened reactivity after stenting (post-stent aggregation > baseline aggregation)  Non-heightened reactivity | Not explicitly reported | heightened reactivity after stenting (post-stent aggregation > baseline aggregation) : NR  Non-heightened reactivity: NR |
| Gurbel, 2005{Gurbel, 2005 215 /id}  16286165  USA  PREPARE POST-STENTING | LTA  Chronology Lumi-Aggregometer (Model 490-4D)  Chronology, Havertown, Pennsylvania | 20um ADP | At discharge  3.8% trisodium citrate  2 hours  NR | High LTA (maximum percent change in light transmittance from baseline) >67%  Not high LTA (maximum percent change in light transmittance from baseline ≤67%) | Defined by ROC curve in the same study | High LTA : NR  Not high LTA : NR |
| Gurbel, 2008{Gurbel, 2008 157 /id}  19012177  USA  None | Conventional aggregometry  Chronolog LumiAggregometer (Model 490-4D) with the Aggrolink software package  Chronolog, Havertown, PA | 5 and 20 uM ADP | Post-procedural blood samples were drawn by venipuncture into vacutainer tubes. The tubes were filled to capacity and gently inverted 3–5 times to ensure complete mixing of the anticoagulant  3.2% trisodium citrate  Platelet function was measured on the day of hospital discharge in patients not treated with eptifibatide or >=5 days post-discharge in patients treated with eptifibatide (all after clopidogrel dosing)  Within 30 minutes | >46% platelet aggregation after 5 umol ADP stimulation (HPR)  ≤46% (no HPR)  >59% platelet aggregation after 20 umol ADP stimulation (HPR)  ≤59% (no HPR) | ROC analysis in present study | >46% platelet aggregation after 5 umol ADP stimulation (HPR): 88 (30%)  ≤46% (no HPR): 209 (70%)  >59% platelet aggregation after 20 umol ADP stimulation (HPR):101 (34%)  ≤59% (no HPR): 196 (66%) |
| Gurbel, 2010{Gurbel, 2010 84 /id}  20194878  10 study sites in North America and Europe  RESPOND | light transmission aggregometry  Chronolog Optical Aggregometer (model 490–4D)  NR | 20 μmol/L ADP | NR  3.2% trisodium citrate  0.25 -0.33 days (6-8 hrs); clopidogrel came first  NR | Nonresponder (absolute change in maximum platelet aggregation (MPA) ≤10% between pre-dose and 6-8 hr post-dose measurements)    Responder (absolute change in maximum platelet aggregation (MPA) >10% between pre-dose and 6-8 hr post-dose measurements) | Based on literature | Nonresponder (absolute change in maximum platelet aggregation (MPA) ≤10% between pre-dose and 6-8 hr post-dose measurements): 41/98 (41.8%)  Responder (absolute change in maximum platelet aggregation (MPA) >10% between pre-dose and 6-8 hr post-dose measurements): 57/98 (58.2%) |
| Hochholzer, 2006{Hochholzer, 2006 208 /id}  17084243  Germany  EXCELSIOR | turbidimetric aggregometry 4-channel Bio/Data PAP4 aggregometer  Mölab, Langenfield, Germany | ADP | blood was drawn for platelet function assays  We obtained the second blood sample at  the time of catheterization before administration of heparin  or contrast medium. 3.8% sodium citrate  NR  NR | Quartiles | NR | Quartiles |
| Hoshino, 2009{Hoshino, 2009 143 /id}  19106460  Japan  NR | light transmission aggregometry  12-channel light transmission aggregometer  MCM HEMA TRACER 313  MC Medical, Japan | 5 and 20 μmol/L ADP | 1) Baseline; 2) 4 h after loading; 3) 24 h after loading; 4) 48 h after loading; 5) 14 days after loading; 6) 28 days after loading  0.313% sodium citrate.  Interval: 0.16 days (4 hrs), 1 day; 2 days; 14 days and 28 days; clopidogrel came first  0.1 days (2 hours) | IPA <10% (clopidogrel non-responders)  10%≤ IPA <30% (hypo-responders)  IPA ≥30% (responders) | Based on a previous report | IPA <10% (clopidogrel non-responders): 4 (14.3%)  10%≤ IPA <30% (hypo-responders): 14 (50%)  IPA ≥30% (responders): 10 (35.7%) |
| Htun, 2011{Htun, 2011 20 /id}  21273381  Germany  NR | turbidimetric aggregometry two-channel Chronolog aggregometer (Nobis, Germany) | ADP | Blood samples for platelet function analysis were  obtained at an earliest time point of 6 hours after  administration of 600 mg of clopidogrel,  NR  Blood samples for platelet function analysis were  obtained at an earliest time point of 6 hours after  administration of 600 mg of clopidogrel, when A minority of patients  already on chronic clopidogrel treatment received  a loading dose of 300 mg and were measured  approximately 24 hours after drug administration. | low responder 326 (20.8)  responder 1009 (64.4)  cutoff is beyond 75 percentile of all value in platelet aggregation as low responder. | Based on literature | low responder 326 (20.8)  responder 1009 (64.4) |
| Kim, 2010{Kim, 2010 241 /id}  20449634  Korea  NR | LTA ADP  AggRam  aggregometer  Helena Laboratories Corp., Beaumont, TX | 5 and 20 μmol/L ADP | Blood samples were drawn into vacutainer tubes containing 0.5 ml of sodium citrate 3.2% and processed within 60 min  sodium citrate 3.2%  clopidogrel- naı¨ve patients received a 300-mg loading-dose (LD) of clopidogrel at least 12 h before procedure, and blood sampling was performed after insertion of the arterial sheath. In the case of patients who were already on chronic clopidogrel therapy, blood sampling was performed at the catheterization lab without clopidogrel LD  60 minutes | Aggregation <50%  Aggregation ≥50% | Based on literature | Aggregation <50%: NR  Aggregation ≥50%: NR |
| L’Allier 2008{L'Allier, 2008 178 /id}  18342223  Canada  PREPAIR study | aggregometry light transmission aggregometer (Model 570VS) Chrono-Log Corporation, Havertown, Pennsylvania | ADP at concentrations of 5 and 20 umol/l | Blood was collected from the forearm citrate 3.2%  Blood samples were obtained at the time of randomization (baseline), immediately before coronary angiography, and the next morning (12 to 24 h) when a PCI was performed (post- PCI) NR | Nonresponders (resistance) to clopidogrel  <10% inhibition of peak aggregation  <20% inhibition of peak aggregation  <40% inhibition of peak aggregation | Based on literature | Nonresponders (resistance) to clopidogrel by 5 umol ADP per liter & 20 umol ADP per liter:  <10% inhibition of peak aggregation 9 in Group A (18%), 8 in Group B (16%), 0 in Group C 11 in Group A (22%), 12 in Group B (24%), 3 in Group C (6%)  <20% inhibition of peak aggregation 16 in Group A (33%), 18 in Group B (37%), 4 in Group C (8%) 21 in Group A (43%), 25 in Group B (51%), 9 in Group C (18%)  <40% inhibition of peak aggregation 30 in Group A (618%), 29 in Group B (59%), 14 in Group C (28%) 38 in Group A (78%), 36 in Group B (73%), 20 in Group C (40%) |
| Liu, 2011{Liu, 2011 12 /id}  21613806  China  None | Turbidometric method in a 4-channel light transmission aggregometer LBY-BJ4 Precil, China | ADP at concentrations of 5 and 20 umol/l | NR  3.8% trisodium citrate  Blood samples were collected before clopidogrel administration (baseline and at 12 h (10-14) and 36 h (34-318) after the loading dose. The 12-hour sample was collected before the daily 75-mg clopidogrel dose, whereas the 36-hour sample was collected afterward  NR | inhibition of platelet aggregation (IPA) with 5 umol ADP at 12 hr: <10% [clopidogrel nonresponders]  35 (32%)  (IPA) < 30% but >/=10% [clopidogrel low responders] 28 (25%)  (IPA) >/=30% [clopidogrel responders] 46 (41%) | Based on literature | inhibition of platelet aggregation (IPA) with 5 umol ADP at 12 hr: <10% [clopidogrel nonresponders]  35 (32%)  (IPA) < 30% but >/=10% [clopidogrel low responders] 28 (25%)  (IPA) >/=30% [clopidogrel responders] 46 (41%) |
| Matetzky,  2004{Matetzky, 2004 188 /id}  15184279  Israel  No | turbidoaggregometry  A routine aggregometer: PACKS-4  Helena Laboratory | ADP, 5 umol/L | NR  Citrate  Blood sampling done before clopidogrel dose (interval NR) and 6 days after  NR | Quartile of % reduction of ADP-induced platelet aggregation at 6 days vs. baseline (before clopidogrel LD)  [P<0.01 among the quartiles for both mean % reduction and inhibition of aggregation) | Not explicitly reported | 1: mean±SD, 103±8% (low responders) : 15 (25%)  2: mean±SD 69±3%: 15 (25%)  3: mean±SD 58±7%: 15 (25%)  4: mean±SD 33±12%: 15 (25%) |
| Muller, 2003{Muller, 2003 223 /id}  12719773  Germany  None | Lumi-aggregometry NR (article says done as previously described and cites ref 7—I skimmed reference and nothing special specified) NR | 5 or 20 umol ADP | NR  citrate  Prior to, 4 and  24 h after clopidogrel administration, whole blood was collected; in some patients, blood was collected 7 and 14 days after PCI  NR | Responder (>30% inhibition of aggregation)  Nonresponder (inhibition <10%)  Semiresponder (inhibition 10-29%) | Not explicitly reported | Response with 5 umol ADP & 20 umol ADP:  Responder (>30% inhibition of aggregation) 90 (86%) 12 (11%)  Nonresponder (inhibition <10%) 5 (5%) 27 (26%)  Semiresponder (inhibition 10-29%) 10 (10%) 66 (63%) |
| Muller, 2010{Muller, 2010 51 /id}  20728084  Germany  NR | light transmission aggregometry  Chronolog Lumi aggregometer  Chronolog, Havertown, Pennsylvania | ADP | NR  3.8% citrate plasma  0.25 -1 day (6-24 hrs); Clopidogrel came first  NR | Stratum I: RPA & CRP <median Stratum II:RPA >median & CRP ≤median Stratum III:RPA ≤ median & CRP >median Stratum IV:RPA & CRP >median | Not explicitly reported | Stratum I: RPA & CRP <median:NR Stratum II:RPA >median & CRP ≤median:NR Stratum III:RPA ≤ median & CRP >median:NR Stratum IV:RPA & CRP >median:NR |
| Obradovic, 2009{Obradovic, 2009 123 /id}  19318922  Serbia  NR | Platelet aggregation  BCT-system  Dade-Behring, Germany | 20 umol/L ADP | Venous blood was sampled in tubes from an antecubital vein under minimal stasis.  3.8% sodium citrate  After the angiogram, patients with one or two vessel disease suitable for PCI were scheduled for PCI 3-4 h later, and these patients received a loading dose of clopidogrel of 300 mg.  Before PCI, 15 min after PCI, 24 h after PCI | High aggregation Low aggregation  Platelet aggregation to ADP above the median was defined as high aggregation and below the median as low aggregation. | not explicitly reported | High aggregation:n=26  Low aggregation:n=26 |
| Saw, 2008{Saw, 2008 243 /id}  19038679  Canada  ELAPSE trial | light-transmittance aggregometry  lumi-aggregometer  Chronolog Corp, Havertown, Pennsylvania | 5 umol/L ADP | Patients were fasting for 4h prior to blood withdrawal. The ﬁrst 3 ml of blood drawn were discarded. Baseline samples were collected from the arterial sheath. Post-PCI samples were drawn from peripheral venipunctures.  EDTA, sodium citrate (3.2%), heparin  Clopidogrel 600 mg was given before stenting. Platelet data measured at baseline (before clopidogrel); 1 day (16-24 hr) after PCI; and 1, 6, and 12 months after  2 h after blood withdrawal in duplicates (means reported as percent aggregation) | Absolute difference between baseline and post-clopidogrel platelet aggregation with LTA using 5.0 umol/l ADP:  <10% (resistance)  ≥10% or greater (nonresistance) | Based on literature | <10% (resistance):4/26 (16%) 1 day after PCI  10% or greater (nonresistance):22/26 (85%) 1 day after PCI |
| Trenk, 2008{Trenk, 2008 171 /id}  18482659  Germany  EXCELSIOR (Impact of Extent of Clopidogrel- Induced Platelet Inhibition During Elective Stent Implantation  on Clinical Event Rate) | light transmission aggregometry  4-channel Bio/ Data PAP4 aggregometer  Mölab, Langenfeld, Germany | 5 and 20 umol ADP | Baseline, cardiac catheterization and at predischarge sample at day 1  3.8% sodium-citrate  0.08 – 0.16 days (2-4 hrs) after clopidogrel  0.04 (1 hour) | high on-treatment platelet reactivity (Residual platelet aggregation >14%)  no high on-treatment platelet reactivity (Residual platelet aggregation ≤14%) | Based on literature | high on-treatment platelet reactivity (Residual platelet aggregation >14%) :217 (28.4%)  no high on-treatment platelet reactivity (Residual platelet aggregation ≤14%):548 (71.6%) |
| Wang, 2009{Wang, 2009 130 /id}  19041120  China  NR | Chrono-Log Lume-Aggregometer  Chrono-Log Lume-Aggregometer (model 700) and the Aggro/Link software package  Chrono-Log Corporation, Havertown, Pennsylvania, USA | 20 umol ADP | The first sample was defined as baseline. Blood samples were collected in evacuated container tubes containing 3.8% trisodium citrate. Tubes were filled to capacity and then inverted 3 to 5 times for gentle mixing.  3.8% trisodium citrate  Patient blood samples were collected before clopidogrel administration, and at least 24 hours after the first 300 mg clopidogrel dose to make sure maximum platelet inhibition has been achieved.  NR | Clopidogrel resistance  Normal clopidogrel response  Drug resistance was defined as 10% or less absolute difference between aggregation at baseline and 24h after the 300mg loading dose of clopidogrel. | Based on literature | Clopidogrel resistance :65/386=16.8%  Normal clopidogrel response :321/386=83.2% |
| Wang, 2010{Wang, 2010 37 /id}  21171668  China  None | light transmittance aggregometry (LTA)  Chrono-Log Lume-Aggregometer (model 700) with Aggro/Link software  Chrono-Log Corpor ation, Havertown, PA | 20 μmol/L ADP | Blood  3.8 % sodium citrate  Before clopidogrel administration (baseline) and at least 24 (24 – 28) hours after loading with clopidogrel 300 mg  NR | Clopidogrel resistance was defined as≤10 % absolute difference between baseline aggregation and post-administration aggregation  Nonresistance (>10%) | Based on literature | Clopidogrel resistance:32 (21%)  Nonresistance (>10%):122 (79%)  :  : |
| Yong, 2009{Yong, 2009 146 /id}  19081397  Australia  Platelet Responsiveness to Aspirin and Clopidogrel and  Troponin Increment after Coronary intervention in Acute  coronary Lesions (PRACTICAL) Trial | light transmission aggregometry  8 sites: Chronolog; 2 sites—Monitor IV Plus  Chronolog instruments, Havertown, PA; Monitor IV Plus, Helena, Beaumont, TX | ADP 4, 10, and 20 μmol/L | before angiography (preangiography sample) and the morning after the procedure (morning-after sample)  Citrate  2 hours  4 hours | Quartiles | not explicitly reported | Quartile cutoffs: NR |
| Kalantzi, 2012{Kalantzi, 2012 18174 /id} 21806493  Greece  NR | light transmission aggregometry  LTA  Chronolog Lumi-Aggregometer (model 560-Ca)  with the AggroLink software package | ADP 2.5, 5 and 10uM  ADP  ADP | Citrated blood samples were collected after the patient’s presentation at the emergency room  before clopidogrel administration (baseline), as well as at 5- and 30-days after clopidogrel loading.  citrate  5 days  30 days | nonresponder  VASP PRI >50%  responder  VASP PRI <50% | reference 15, 23 | nonresponder n=12  responder n=28 |
| Angiolillo, 2011 {Angiolillo, 2011 18175 /id}  Italy  NR | light transmittance aggregometry (LTA)  NR | ADP 20uM | NR  NR  NR  NR | HPR=upper quartile of ADP induced aggregation (64%) | reference 9, 17, 18 | HPR N=47  no HPR N=140 |
| Park, 2011 {Park, 2011 1 /id} 22152948  Korea  NR | VerifyNow P2Y12  NR  NR | ADP | NR  NR  NR  NR | HTPR =PRU >235 | references 13-15 | high n=1660  normal n=1189 |
| Gurbel, 2012{Gurbel, 2012 18183 /id} 21862113  USA  NR | light transmittance aggregometry  LTA  NR | ADP (5 and 20μM)  and 4 μg/ml collagen | blood samples at baseline, 2, 6 and 24 hours post 600 mg clopidogrel  3.2% trisodium citrate  2, 6 and 24 hours (0-6 hr time used to define responsiveness) | Clopidogrel resistance (nonresponse) ≤10% absolute change in 20μM ADP-induced aggregation between baseline and  6 hours post-dose. | NR | Nonresponders=21 (27%)  Responders=57 (73%) |
| Saad, 2012{Saad, 2012 18187 /id}  22146578  Egypt  NR | light transmittance aggregometry  Chronolog LumiAggregometer (Model 450) Chronolog, Havertown, PA | ADP (5 μM) | Peripheral blood samples before PCI 6 hrs after clopodigrel  3.8% trisodium citrate  0.25 days (6hours)  NR | best cutoff value of posttreatment platelet  reactivity to predict ischemic events | ROC analysis | NR |
| Aradi {Aradi, 2012 18248 /id}  21902692  Hungary  NR | CARAT TX4 four-channel light transmission aggregometer  (Carat Diagnostics, Budapest, Hungary) | ADP (5uM) | NR  NR  NR  2 hours | normal platelet reactivity (NPR ) LTA adp <34% n=122  high on-clopidogrel platelet reactivity (HPR)  LTAadp≥34% n=78 | ref 14 and 15 | NPR N=122  HPR N=78 |
| Gaglia, 2012{Gaglia, 2011 18244 /id}  21919956  USA  NR | LTA  light transmission aggregometry  ChronoLog, Havertown, PA, USA | 5 and 20 μM of adenosine disphosphate  (ADP) | 6 hours following a loading  dose of clopidogrel  3.2% sodium citrate  6 hours  6 and 24 hours following PCI | MPA >46% for LTA with 5 μM ADP  MPA ≤46% for LTA with 5 μM ADP  MPA >60% for LTA with 20 μM ADP  MPA ≤60% for LTA with 20 μM ADP | Based on literature | 5 μM ADP  MPA >46% : 46  MPA ≤46%: 154  20 μM ADP  MPA >60% : 32  MPA ≤60%: 168 |
| Marcucci, 2012{Marcucci, 2012 18217 /id}  22390861  Italy  NR | LTA  APACT 4 light transmission aggregometer Helena Laboratories, Milan, Italy | 10 μM of ADP | Whole blood  NR  NR  NR | high on-treatment platelet reactivity (HPR)  MPA ≥55% for LTA with 10 μM ADP  MPA <55% for LTA with 10 μM ADP | Based on literature | Entire cohort  MPA ≥55% : 486  MPA <55%: 701  in CYP2C19 carriers  MPA ≥55% : 144  MPA <55%: 151  in CYP2C19 noncarriers  MPA ≥55% : 342  MPA <55%: 550 |
| Ge, 2012{Ge, 2012 18184 /id}  21602258  China  NR | LTA  Chrono-Log Lume-Aggregometer (model 700); Aggro/Link software package (Chrono-Log Corporation, Havertown, Pennsylvania) | 5 μM of ADP | Whole blood to obtain plasma  NR  From baseline to “loading”  NR | “resistance”: ≤10% drop in reactivity between baseline and post-loading  “non-resistance” >10% drop in reactivity between baseline and post-loading | Based on literature | ≤10% drop in reactivity between baseline and post-loading: 65  >10% drop in reactivity between baseline and post-loading: 287 |

\*If more than one test, they are presented in separate rows

ADP= adenosine 5'-diphosphate; Ag= aggregation; PGE1=prostaglandin; ROC=receiver operating characteristic; AUC=area under the curve; IPA= inhibition of platelet aggregation; LTA= light transmission aggregometry; MEA= multiple electrode platelet aggregometry; PFA= platelet function analysis; TEG=thromboelastography; sTEG=short thromboelastography; VASP = vasodilator-stimulated phosphoprotein; VASP-FCT=vasodilator-stimulated phosphoprotein flow cytometry; CEPI=collagen-epinephrine ; CADP=collagen-ADP; CT=closure times; HCPR=high on-clopidogrel platelet reactivity; PCI = percutaneous coronary intervention; RPA= residual platelet aggregation; GP= glycoprotein; HRP=high platelet reactivity; NPR=normal on-treatment platelet reactivity; HPPR= high post-treatment platelet reactivity; MPA= maximum platelet aggregation; RPR= residual platelet reactivity; OTPR=on-treatment platelet reactivity; DPAI= degree of platelet aggregation inhibition; PRU=P2Y12 reaction units; CRP=C-reaction protein; PRI=platelet reactivity index; LR=low responder; IQR=interquartile range; AA= arachidonic acid; LD=loading dose; MD=maintain dose; SD=standard deviation; NR=not reported;