**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}17936152SpainNR | Light transmittance aggregometry ChronoLog 490ModelChronoLog Corp., Havertown, Pennsylvania | ADP | Blood samples for platelet function assays were collected 2 to 4 h after antiplatelet therapy intakeNR2 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}18388039HungaryNR | Optical aggregometryCarat 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 tubeSodium citrateClopidogrel given at time of PCI and stenting and platelets tested at 30 ± 5 days after coronary stent implantation2 hours | Lower 50% of ADP 5 umol Induced AggregationUpper 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}20170822FranceALBION (Assessment of the Best Loading Dose of Clopidogrel to Blunt Platelet Activation, Inflammation and Ongoing Necrosis) | LTANRNR | 20 µmol/l ADP | Samples obtained at baseline and 0.5, 1, 2, 3, 4, 5, 6, and 24 hNRLess 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}17291930USANR | Platelet aggregation/Chronolog Lumi-Aggregometer Model 490-4DChronolog, 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 heparinBaseline samples were obtained before coronary intervention and at 3 h and 18 to 24 h after stentingWithin 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 GermanyNR | Platelet aggregation /Densitometrically-determined measurement of platelet aggregation APACT 4 SPlus 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 days3.2% citrateAll 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 daysWithin 1 h | NR | NR | NR |
| Breet, 2010{Breet, 2010 50 /id}20695984NetherlandsSubstudy of a larger cohort (Breet 2010 PMID: 20179285) | LTAfour-channel APACT 4004aggregometerLABiTec, Arensburg, Germany | NR | NR3.2% citrateNR2h | 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}20179285NetherlandsPOPULAR | Light transmittance aggregometry NRNR | 5 µmol/L ADP20 µmol/L ADP | Before Heparinization3.2% citrateNRWithin 2 hours after blood collection. | High on-treatment platelet reactivity ≥42.9% aggregation LTA-ADP 5 µmol/L N=445Not High on-treatment platelet reactivity <42.9% aggregation LTA-ADP 5 µmol/L N=604High on-treatment platelet reactivity <64.5% aggregation LTA-ADP 20 µmol/L n=659Not 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=445Not High on-treatment platelet reactivity <42.9% aggregation LTA-ADP 5 µmol/L: N=604High 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}21478385The NetherlandsPOPular | Light transmission aggregometryFour-channel APACT 4004 aggregometerLABiTec, Arensburg, Germany | ADP | NR3.2% Sarstedt citrateNR2h | 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): 536With HCPR (LTA5): 385No HCPR (LTA20): 588With HCPR (LTA20): 335 |
| Buonamici, 2007{Buonamici, 2007 200 /id}17572245ItalyNR | 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 loading0.129 mol/l sodium citrate12-18 h from clopidogrel loadingNR | RespondersNon-respondersPatients 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}17868803ItalyNR | Platelet aggregation NRNR | ADP | NRNRT0 baseline before thienopyridine;T1, 5-7 days after baseline;T2, 7-10 days after T1NR | Responder to both thienopyridinesClopidogrel nonrespondersTiclopidine nonresponders Nonresponder to both thienopyridines[Based on thienopyridine responsiveness] | Not explicitly reported | Responder to both thienopyridines: 90Clopidogrel nonresponders: 30Ticlopidine nonresponders: 28Nonresponder to both thienopyridines: 5 |
| Cuisset, 2006{Cuisset, 2006 212 /id}16371119FranceNR | light transmittancePAP4 AggregometerBiodata 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 mixing3.8% Trisodium citratebefore the PCI at least 12 h after the loading dose of clopidogrel and the aspirin administration and before administration of tiroﬁban if neededImmediately | Quartiles of (mean ± SD) ADP-induced maximal intensity of platelet aggregation (with threshold for low response ≥70%)Q1, Q2, and Q3: responsive to clopidogrelQ4 (82 ± 1 2%): nonresponsive to clopidogrel | The quartile data—Q4 range determined the cutoff | Q1, Q2, and Q3: responsive to clopidogrel: 83Q4 (82 ± 1 2%): nonresponsive to clopidogrel: 23 |
| Cuisset, 2006{Cuisset, 2006 237 /id}17010792FranceNR | Light transmissionPAP4 AggregometerBiodata Corporation, Wellcome, Paris, France | 10 µmol/L ADP | Before PCI after clopidogrel LD3.8% trisodium citrate0.5 days (12 hours)Clopidogrel came firstNR | high post treatment platelet reactivity (ADP induced platelet aggregation >70%) in 300 mg groupnormal 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 groupnormal 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}17264958FranceNR | Light transmissionPAP4 AggregometerBiodata Corporation, Wellcome, Paris, France | ADP | Blood samples for testing platelet reactivity were drawn in the catheterization laboratory from a 6-French arterial sheath beforethe PCI3.8% trisodium citrateBlood samples were drawn before the PCI, at least 12 h after the loading dose of clopidogrel and aspirin, and before administration of tirofiban if neededNR | HPPR ADP10 >70No 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}19801028FranceNR | light transmission aggregometry PAP4 aggregometerBio data welcome, Paris France | 10 umol/LADP | blood samples were obtained 72–96 h after stent placementCitrate 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}19736156FranceNR | Light transmission aggregometry PAP4 Aggregometer Biodata Corporation, Wellcome, Paris, Francea | ADP | Blood drawn after cardiac catheterizationNR0.5 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}17938809FranceNR | light transmission aggregometry PAP4 aggregometerBio 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}17949474GermanyNR | TurbidoaggregometryChronolog Lumi aggregometer with Aggro-link softwareNR | 20 umol ADP | Venous blood. RPA measured 5 min after ADP addition3.8% citrateAt 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 doseNR | RPA tertile 1 (lowest)RPA tertile 2RPA tertile 3 (highest) | Not explicitly reported | RPA tertile 1 (lowest) NRRPA tertile 2 NRRPA tertile 3 (highest) NR |
| Geisler 2010{Geisler, 2010 54 /id}20526607GermanyNR | Turbidometry;Chronolog Lumi Aggregometer Chronolog | ADP (20 umol/l) | NRSamples were collected the day following PCIblood was collected at least 6 h (median 23.6 h interquartile range 20.8 h) after first administration of 600 mg clopidogrelNR | 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}17005534GermanyNR | NRChronolog Lumi aggregometer with Aggro-LinkSoftwareNR | ADP | Blood samples were collected in 3.8%citrate plasma3.8% citrate plasmaPatient blood was collected at least 6 h (mean 34.8+25.9 h) after first administration of 600 mg clopidogrelNR | 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}19812059GermanyNR | light transmission aggregometryChronolog Lumi aggregometerNR | ADP | 6 hrs after clopidogrel dose3.8% citrate0.25 days (6 hours); Clopidogrel came firstNR | 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}19268736ItalyRECLOSE study(Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | Turbidimetric aggregometryAPACT4 (4 channel aggregometer)Helena Laboratories (Milan, Italy) | ADP (10 μM) | Venous blood was obtainedCitrated bloodVenous blood was obtained 12-18 h from clopidogrel loading; for patients administered IIb/IIIa inhibitors blood was obtained 6 d after catheterizationNR | 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}19132241Italy RECLOSE | LTA/NRAPACT 4 light transmittance aggregometerHelena Laboratories, Milan, Italy | 10 umol ADP or 2 μg/ml collagen | NR0.109 M sodium citratePlatelet 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 clopidogrelNR | All patients RPR ≥70% by LTA with ADPNo RPRRPR by LTA with collagen >90th percentile of patients’ distribution No RPRRPR 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 literatureLTA-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}18718420ItalyRECLOSE study(Low Responsiveness to Clopidogrel and Sirolimus- or Paclitaxel-Eluting Stent Thrombosis) | light transmission aggregometryAPACT4HelenaLaboratories, Milan, Italy | 10-μM ADP (clopidogrel) , 1-mM arachidonic acid (aspirin), and 2-μg/ml collagen (clopidogrel) | In catheterization laboratory0.129 mol/l sodium citrate0.5-0.75 day (12 to 18 h ); 6 days for those pm glycoprotein (GP) IIb/IIIa inhibitorclopidogrel came firstNR | 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}20691842USAPREPARE POST-STENTING | light transmission aggregometryLumiAggregometer 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 citrateNR; Clopidogrel came firstNR | Quartile of LTA with ADP Quartile 1 <25 %Quartile 2 25-35 %Quartile 3 >35-45 %Quartile 4 >45 % | Quartiles: Not explicitly reportedAlso 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}12796140USANR | LTAChronology Lumi-Aggregometer (Model 490-4D)Chronology, Havertown, Pennsylvania | 5 μm ADP | Response assessed at day 53.8% trisodium citrate2 hoursNR | Drug resistance= <10% difference between baseline aggregation and posttreatment aggregation with 5 μmol/L ADP used as the agonist | Based on literature | ResistanceNonresistance |
| Gurbel, 2003{Gurbel, 2003 224 /id}12714161USANR | Platelet aggregation NRNR& P-selectin expression by flow cytometryNRParmingen, San Diego, California | ADP 5 and 20 umol/liter for LTA & ADP 200 umol/liter for Flow cytometry | Blood was collected in vacutainer tubes3.8% trisodium citrateBlood 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}15154601USANone | aggregometryChronolog Lumi-Aggregometer (model 4902D) with AggroLink softwareChronolog, 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 mixing3.8% trisodium citrateobtained before clopidogrel administration and stenting (baseline); and at 2 h, 24 h, 5 days and 30 days post-stentingNR | 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}16286165USAPREPARE POST-STENTING | LTAChronology Lumi-Aggregometer (Model 490-4D)Chronology, Havertown, Pennsylvania | 20um ADP | At discharge3.8% trisodium citrate2 hoursNR | 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 : NRNot high LTA : NR |
| Gurbel, 2008{Gurbel, 2008 157 /id}19012177USANone | Conventional aggregometryChronolog LumiAggregometer (Model 490-4D) with the Aggrolink software packageChronolog, 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 anticoagulant3.2% trisodium citratePlatelet 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}2019487810 study sites in North America and EuropeRESPOND | light transmission aggregometryChronolog Optical Aggregometer (model 490–4D)NR | 20 μmol/L ADP | NR3.2% trisodium citrate0.25 -0.33 days (6-8 hrs); clopidogrel came firstNR | 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}17084243GermanyEXCELSIOR | turbidimetric aggregometry 4-channel Bio/Data PAP4 aggregometer Mölab, Langenfield, Germany | ADP | blood was drawn for platelet function assaysWe obtained the second blood sample atthe time of catheterization before administration of heparinor contrast medium. 3.8% sodium citrateNR NR | Quartiles | NR | Quartiles |
| Hoshino, 2009{Hoshino, 2009 143 /id}19106460JapanNR | light transmission aggregometry 12-channel light transmission aggregometerMCM HEMA TRACER 313MC 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 loading0.313% sodium citrate.Interval: 0.16 days (4 hrs), 1 day; 2 days; 14 days and 28 days; clopidogrel came first0.1 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}21273381GermanyNR | turbidimetric aggregometry two-channel Chronolog aggregometer (Nobis, Germany) | ADP | Blood samples for platelet function analysis wereobtained at an earliest time point of 6 hours afteradministration of 600 mg of clopidogrel, NRBlood samples for platelet function analysis wereobtained at an earliest time point of 6 hours afteradministration of 600 mg of clopidogrel, when A minority of patientsalready on chronic clopidogrel treatment receiveda loading dose of 300 mg and were measuredapproximately 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}20449634KoreaNR | LTA ADPAggRamaggregometer 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 minsodium 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 LD60 minutes | Aggregation <50%Aggregation ≥50% | Based on literature | Aggregation <50%: NRAggregation ≥50%: NR |
| L’Allier 2008{L'Allier, 2008 178 /id}18342223CanadaPREPAIR 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}21613806ChinaNone | 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 citrateBlood 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}15184279Israel No | turbidoaggregometryA routine aggregometer: PACKS-4Helena Laboratory | ADP, 5 umol/L | NRCitrateBlood sampling done before clopidogrel dose (interval NR) and 6 days afterNR | 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}12719773GermanyNone | 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 citratePrior to, 4 and24 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}20728084GermanyNR | light transmission aggregometryChronolog Lumi aggregometerChronolog, Havertown, Pennsylvania | ADP | NR3.8% citrate plasma0.25 -1 day (6-24 hrs); Clopidogrel came firstNR | Stratum I: RPA & CRP <medianStratum II:RPA >median & CRP ≤medianStratum III:RPA ≤ median & CRP >medianStratum IV:RPA & CRP >median | Not explicitly reported | Stratum I: RPA & CRP <median:NRStratum II:RPA >median & CRP ≤median:NRStratum III:RPA ≤ median & CRP >median:NRStratum IV:RPA & CRP >median:NR |
| Obradovic, 2009{Obradovic, 2009 123 /id}19318922SerbiaNR | Platelet aggregationBCT-systemDade-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 aggregationLow aggregationPlatelet aggregation to ADP above the median was defined as high aggregation and below the median as low aggregation.  | not explicitly reported | High aggregation:n=26Low aggregation:n=26 |
| Saw, 2008{Saw, 2008 243 /id}19038679CanadaELAPSE trial | light-transmittance aggregometrylumi-aggregometerChronolog 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%), heparinClopidogrel 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 after2 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 PCI10% or greater (nonresistance):22/26 (85%) 1 day after PCI |
| Trenk, 2008{Trenk, 2008 171 /id}18482659GermanyEXCELSIOR (Impact of Extent of Clopidogrel- Induced Platelet Inhibition During Elective Stent Implantationon Clinical Event Rate) | light transmission aggregometry4-channel Bio/ Data PAP4 aggregometerMölab, Langenfeld, Germany | 5 and 20 umol ADP | Baseline, cardiac catheterization and at predischarge sample at day 13.8% sodium-citrate0.08 – 0.16 days (2-4 hrs) after clopidogrel0.04 (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}19041120ChinaNR | Chrono-Log Lume-AggregometerChrono-Log Lume-Aggregometer (model 700) and the Aggro/Link software packageChrono-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 citratePatient 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}21171668ChinaNone | light transmittance aggregometry (LTA)Chrono-Log Lume-Aggregometer (model 700) with Aggro/Link softwareChrono-Log Corpor ation, Havertown, PA | 20 μmol/L ADP | Blood3.8 % sodium citrateBefore clopidogrel administration (baseline) and at least 24 (24 – 28) hours after loading with clopidogrel 300 mgNR | Clopidogrel resistance was defined as≤10 % absolute difference between baseline aggregation and post-administration aggregationNonresistance (>10%) | Based on literature | Clopidogrel resistance:32 (21%)Nonresistance (>10%):122 (79%):: |
| Yong, 2009{Yong, 2009 146 /id}19081397AustraliaPlatelet Responsiveness to Aspirin and Clopidogrel andTroponin Increment after Coronary intervention in Acutecoronary Lesions (PRACTICAL) Trial | light transmission aggregometry8 sites: Chronolog; 2 sites—Monitor IV PlusChronolog 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)Citrate2 hours4 hours | Quartiles | not explicitly reported | Quartile cutoffs: NR |
| Kalantzi, 2012{Kalantzi, 2012 18174 /id} 21806493GreeceNR | light transmission aggregometryLTAChronolog Lumi-Aggregometer (model 560-Ca)with the AggroLink software package | ADP 2.5, 5 and 10uMADPADP | Citrated blood samples were collected after the patient’s presentation at the emergency roombefore clopidogrel administration (baseline), as well as at 5- and 30-days after clopidogrel loading. citrate5 days 30 days | nonresponderVASP PRI >50%responder VASP PRI <50% | reference 15, 23 | nonresponder n=12responder n=28 |
| Angiolillo, 2011 {Angiolillo, 2011 18175 /id}ItalyNR | light transmittance aggregometry (LTA)NR | ADP 20uM | NRNRNRNR | HPR=upper quartile of ADP induced aggregation (64%) | reference 9, 17, 18 | HPR N=47no HPR N=140 |
| Park, 2011 {Park, 2011 1 /id} 22152948KoreaNR | VerifyNow P2Y12NRNR | ADP | NRNRNRNR | HTPR =PRU >235  | references 13-15 | high n=1660normal n=1189 |
| Gurbel, 2012{Gurbel, 2012 18183 /id} 21862113USANR | light transmittance aggregometryLTANR | ADP (5 and 20μM)and 4 μg/ml collagen | blood samples at baseline, 2, 6 and 24 hours post 600 mg clopidogrel3.2% 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 and6 hours post-dose. | NR | Nonresponders=21 (27%)Responders=57 (73%) |
| Saad, 2012{Saad, 2012 18187 /id}22146578EgyptNR | light transmittance aggregometryChronolog LumiAggregometer (Model 450) Chronolog, Havertown, PA | ADP (5 μM) | Peripheral blood samples before PCI 6 hrs after clopodigrel3.8% trisodium citrate 0.25 days (6hours)NR | best cutoff value of posttreatment plateletreactivity to predict ischemic events | ROC analysis | NR |
| Aradi {Aradi, 2012 18248 /id}21902692HungaryNR | CARAT TX4 four-channel light transmission aggregometer(Carat Diagnostics, Budapest, Hungary) | ADP (5uM) | NRNRNR2 hours | normal platelet reactivity (NPR ) LTA adp <34% n=122high on-clopidogrel platelet reactivity (HPR)LTAadp≥34% n=78 | ref 14 and 15 | NPR N=122HPR N=78 |
| Gaglia, 2012{Gaglia, 2011 18244 /id}21919956USANR | LTAlight transmission aggregometryChronoLog, Havertown, PA, USA | 5 and 20 μM of adenosine disphosphate(ADP) | 6 hours following a loadingdose of clopidogrel3.2% sodium citrate6 hours6 and 24 hours following PCI | MPA >46% for LTA with 5 μM ADPMPA ≤46% for LTA with 5 μM ADPMPA >60% for LTA with 20 μM ADPMPA ≤60% for LTA with 20 μM ADP | Based on literature | 5 μM ADPMPA >46% : 46MPA ≤46%: 15420 μM ADPMPA >60% : 32MPA ≤60%: 168 |
| Marcucci, 2012{Marcucci, 2012 18217 /id}22390861ItalyNR | LTA APACT 4 light transmission aggregometer Helena Laboratories, Milan, Italy | 10 μM of ADP | Whole bloodNRNRNR | high on-treatment platelet reactivity (HPR)MPA ≥55% for LTA with 10 μM ADPMPA <55% for LTA with 10 μM ADP  | Based on literature | Entire cohort MPA ≥55% : 486MPA <55%: 701in CYP2C19 carriersMPA ≥55% : 144MPA <55%: 151in CYP2C19 noncarriersMPA ≥55% : 342MPA <55%: 550 |
| Ge, 2012{Ge, 2012 18184 /id}21602258ChinaNR | LTAChrono-Log Lume-Aggregometer (model 700); Aggro/Link software package (Chrono-Log Corporation, Havertown, Pennsylvania) | 5 μM of ADP | Whole blood to obtain plasmaNRFrom 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;