**Appendix Table E20. Results from studies assessing the ability of LTA to predict other clinical events 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)** |
| Bliden,  2007{Bliden, 2007 202 /id}  17291930  USA  NR | clopidogrel  75 mg qd | ADP-induced platelet reactivity | Target vessel revascularization | Target vessel revascularization | Day 0-30 | HPR n=22 | Target vessel revascularization | 0/22 | OR (calculated)=14.25 | 2.6-77.1 | P=0.001  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  | Day 0-30 | NPR  N=78 | Target vessel revascularization | 0/78 | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | Day 31-365 | HPR n=22 | Target vessel revascularization | 6/22 |  |  |  |  |  |  |
|  |  |  |  |  | Day 31-365 | NPR  N=78 | Target vessel revascularization | 2/78 |  |  |  |  |  |  |
|  | clopidogrel  75 mg qd | ADP-induced platelet reactivity | Nontarget vessel revascularization | Nontarget vessel revascularization | Day 0-30 | HPR n=22 | Nontarget vessel revascularization | 0/22 | OR(calculated)=7.7 | 0.7-89.3 | P=0.12  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  | Day 0-30 | NPR  N=78 | Nontarget vessel revascularization | 0/78 | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | Day 31-365 | HPR n=22 | Nontarget vessel revascularization | 2/22 |  |  |  |  |  |  |
|  |  |  |  |  | Day 31-365 | NPR  N=78 | Nontarget vessel revascularization | 1/78 |  |  |  |  |  |  |
|  | clopidogrel  75 mg qd | ADP-induced platelet reactivity | Rehospitalization for ischemia | Rehospitalization for ischemia | Day 0-30 | HPR n=22 | Rehospitalization for ischemia | 2/100 | OR(calculated)=5.6 | 1.1-27 | P=0.04  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  | Day 0-30 | NPR  N=78 | Rehospitalization for ischemia | 0/100 | NR | NR | NR | NR | NR |  |
|  |  |  |  |  | Day 31-365 | HPR n=22 | Rehospitalization for ischemia | 2/100 |  |  |  |  |  |  |
|  |  |  |  |  | Day 31-365 | NPR  N=78 | Rehospitalization for ischemia | 3/100 |  |  |  |  |  |  |
| Campo, 2007{Campo, 2007 197 /id}  17868803  Italy  NR | Clopidogrel 300-mg loading dose, followed by 75 mg/day | LTA ADP | TVR | TVR | 6 months | Responder to both | TVR | 23 | 1/90(1.1) | OR(calculated)=1.95 | 0.3-11.2 | P=0.605  (clopidogrel + dual nonresponder vs responder)  [Fisher’s exact test] | NR |  |
|  |  |  |  |  |  | Clopidogrel nonresponders  Ticlopidine responders |  |  | 2/25(8) |  |  |  |  |  |
|  |  |  |  |  |  | Clopidogrel responders  Ticlopidine nonresponders |  |  | 3/23(13) |  |  |  |  |  |
|  |  |  |  |  |  | Nonresponder to both |  |  | 0/5 |  |  |  |  |  |
| Gurbel, 2008{Gurbel, 2008 157 /id}  19012177  USA  None | Clopidogrel+aspirin | 5 uM ADP aggregation | revascularization (target vessel) |  | 1 mo | >46% platelet aggregation (HPR) |  | 1 | NR | OR(calculated)=7.39 | 3.1-17.5 | P<0.0001  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |
|  |  |  |  |  |  | <=46% |  | 0 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo | >46% platelet aggregation (HPR) |  | 19 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | <=46% |  | 8 | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 5 uM ADP aggregation | revascularization (nontarget vessel) |  | 1 mo | >46% platelet aggregation (HPR) |  | 0 | NR | OR(calculated)=4.34 | 1.5-12.3 | P=0.008  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |
|  |  |  |  |  |  | <=46% |  | 1 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo | >46% platelet aggregation (HPR) |  | 10 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | <=46% |  | 5 | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 5 uM ADP aggregation | Rehospitalization for ischemia, no revascularization |  | 1 mo | >46% platelet aggregation (HPR) |  | 1 | NR | OR(calculated)=3.14 | 1.3-7.6 | P=0.01  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |
|  |  |  |  |  |  | <=46% |  | 1 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo | >46% platelet aggregation (HPR) |  | 11 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | <=46% |  | 9 | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 20 uM ADP aggregation | revascularization (target vessel) |  | 1 mo | >46% platelet aggregation (HPR) |  | 1 | NR | OR(calculated)=3.17 | 1.4-7.1 | P=0.005  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |
|  |  |  |  |  |  | <=46% |  | 0 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo | >46% platelet aggregation (HPR) |  | 16 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | <=46% |  | 11 | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 20 uM ADP aggregation | revascularization (nontarget vessel) |  | 1 mo | >46% platelet aggregation (HPR) |  | 0 | NR | OR(calculated)=4.66 | NR | P=0.004  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |
|  |  |  |  |  |  | <=46% |  | 1 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo | >46% platelet aggregation (HPR) |  | 11 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | <=46% |  | 4 | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 20 uM ADP aggregation | Rehospitalization for ischemia, no revascularization |  | 1 mo | >46% platelet aggregation (HPR) |  | 1 | NR | OR(calculated)=4.71 | 1.9-12 | P=0.0007  (HPR vs NPR)  [Fisher’s exact test] | NR | NR |
|  |  |  |  |  |  | <=46% |  | 1 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo | >46% platelet aggregation (HPR) |  | 14 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | <=46% |  | 6 | NR | NR | NR | NR | NR | NR |
| Liu, 2011{Liu, 2011 12 /id}  21613806  China  None | Clopidogrel+aspirin | Aggregometry | Acute coronary syndrome | presence of symptoms compatible with recurrent ischemia requiring hospitalization and angiocoronarography | 1 month | Nonrespoders | 34 | 1 |  | OR(calculated)=15.2 | 1.8-132.2 | P=0.004  (HPR vs NPR)  [Fisher’s exact test] |  |  |
|  |  |  |  |  |  | Low responders | 28 | 1 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responders | 44 | 0 |  |  | 0.447 across this and previous 2 rows (chi-square test) |  |  |  |
|  | Clopidogrel+aspirin | Aggregometry | Acute coronary syndrome | presence of symptoms compatible with recurrent ischemia requiring hospitalization and angiocoronarography | 3 month | Nonrespoders | 34 | 6 |  |  |  |  |  |  |
|  |  |  |  |  |  | Low responders | 28 | 1 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responders | 44 | 0 |  |  | 0.006 across this and previous 2 rows (chi-square test) |  |  |  |
| 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) | 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 | target lesion intervention | target lesion intervention | 1 year | high on-treatment platelet  reactivity (RPA>14%) | target lesion intervention | 26/217 (12%) | HR=1.1 | 0.7-1.8 | P=0.67 (between high and not high residual platelet reactivity) | 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 platelet  reactivity (RPA≤ 14%) |  | 60/548 (10.9%) |  |  |  |  |  |  |
| Wang, 2010{Wang, 2010 37 /id}  21171668  China  None | Clopidogrel+aspirin | LTA | Revascularization |  | 1 year | Clopidogrel resistance |  | 2 (6.25%) | OR=4.0(calculated) | 0.5-29.6 | 0.191 vs. next row (Student’s t) | NR |  |  |
|  |  |  |  |  |  | nonresistance |  | 2 (1.64%) |  |  |  |  |  |  |
| Gurbel, 2003{Gurbel, 2003 222 /id}  12796140  USA  NR | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | target-vessel revascularization | target-vessel revascularization | 30 days | Clopidogrel resistance | target-vessel revascularization | 0 | NR | OR(calculated)=1.25 | P=0.91  (resistant vs nonresistant)  [Chisquare test] | NR | NO |  |
|  |  |  |  |  |  | Clopidogrel nonresistance |  | 0 |  |  |  |  |  |  |
| Aradi {Aradi, 2012 18248 /id}  21902692  Hungary  NR | LD clopidogrel 600mg and aspirin 300mg  MD clopidogrel 75 mg/day 4 weeks | LTA ADP | TVR | target vessel revascularization | 12 months | NPR | TVR | 9/122=9.5% | OR=1.9 | 0.60-6.07 | NR | NR | NR | NR |
|  |  |  |  |  |  | HPR+150 mg clopidogrel | TVR | 1/36=3.1% |  |  | 0.09 comparing with the low row  log-rank test |  |  |  |
|  |  |  |  |  |  | HPR +75 mg clopidogrel | TVR | 5/38=16.4% |  |  |  |  |  |  |