**Appendix Table E19. Results from studies assessing the ability of LTA to predict stroke 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)** |
| Breet,  2010{Breet, 2010 86 /id}  20179285  Netherlands  POPULAR | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily | ADP LTA 5µmol/L | stroke | Stroke | 1-year | High OTPR  N=445 | Stroke | 6 (1.3) | OR=1.17 | 0.39-3.49 | <0.78  (high vs normal)  [logistic regression] | No | NR |  |
|  |  |  |  |  |  | Normal  OTPR  N=604 |  | 7 (1.2) |  |  |  |  |  |  |
|  | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily | ADP LTA 20 µmol/L | stroke | Stroke | 1-year | High OTPR  N=392 | Stroke | 5 (1.3) | OR=1.05 | 0.34-3.24 | <0.93  (high vs normal)  [logistic regression] | No | NR |  |
|  |  |  |  |  |  | Normal  OTPR  N=659 |  | 8 (1.2) |  |  |  |  |  |  |
| Kim, 2010{Kim, 2010 241 /id}  20449634  Korea  NR | 300-600mg LD and 75 mg maintain dose clopidogrel | 5umol/L ADP LTA | ischemic stroke | ischemic stroke | 6 months | <50% | ischemic stroke | 0.2% | OR=1.58 | 0.10-25.36 | 1.000  (<50 vs ≥ 50%)  [logistic regression] | NR | NR |  |
|  |  |  |  |  |  | ≥50% |  | 1.2% |  |  |  |  |  |  |
| Bliden,  2007{Bliden, 2007 202 /id}  17291930  USA  NR | clopidogrel  75 mg qd | ADP-induced platelet reactivity | Stroke | Stroke | Day 0-30 | HPR n=22 | Stroke | 0 | OR (calculated)=16.1 | NR | P=0.535 (HPR vs NPR at 1 year)  [chi square] | NR | NR |  |
|  |  |  |  |  | Day 0-30 | NPR  N=78 | Stroke | 0 |  |  |  |  |  |  |
|  |  |  |  |  | Day 31-365 | HPR n=22 | Stroke | 0 | OR=3.5 | NR | NR | NR | NR |  |
|  |  |  |  |  | Day 31-365 | NPR  N=78 | Stroke | 0 |  |  |  |  |  |  |
| Breet, 2011{Breet, 2011 15 /id}  21478385  The Netherlands  POPular | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | LTA5 | Stroke | Stroke | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR  N=385 | Stroke | 5 | NR | NR | NR | NR | NR |  |
|  | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | LTA20 | Stroke | Stroke | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR  N=335 | Stroke | 3 | NR | NR | 0.045 comparing with NPR(normal on-treatment platelet reactivity) | NR | NR |  |
| Geisler, 2006{Geisler, 2006 210 /id}  17005534  Germany  NR | Clopidogrel LD dose of 600 mg followed 75 mg daily | ADP LTA | Stroke | Stroke | 3-month | Adequate response  N=341 | Stroke | 5 (1.5) | NR | NR | 0.43  (adequate vs low response)  [Chi square] | NR | NR |  |
|  |  |  |  |  |  | Low response  N=22 |  | 0 |  |  |  |  |  |  |
| Geisler, 2010{Geisler, 2010 101 /id}  19812059  Germany  NR | Clopidogrel 300-600 mg LD + 75 mg MD & Aspirin 500 mg LD + 100 mg MD | LTA | ischemic stroke | NR | 3 months | Low responder (Terrtile 3) | ischemic stroke | 6 (0.9%) | OR=0.7 | 0.14-3.48 | p=0.66  (low responder vs responder)  [chi square] | NO | NR | Secondary outcome |
|  |  |  |  |  |  | Responders (Tertile 1&2) |  | 2 (0.6%) |  |  |  |  |  |  |
| Gurbel, 2008{Gurbel, 2008 157 /id}  19012177  USA  None | Clopidogrel+aspirin | 5 uM ADP aggregation | Stroke |  | 1 mo | >46% platelet aggregation (HPR) |  | 0 | OR (calculated)=12.1 | 0.6-254.9 | P=0.09 (HPR vs NPR at 2 year)  [Fishers exact] | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 1 mo | <=46% |  | 0 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 0 | NR | NR | NR | NR | NR | NR |
|  | Clopidogrel+aspirin | 20 uM ADP aggregation | Stroke |  | 1 mo | >46% platelet aggregation (HPR) |  | 0 | OR (calculated)=9.9 | 0.5-207.7 | P=0.12 (HPR vs NPR at 2 year)  [Fishers exact] | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 1 mo | <=46% |  | 0 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  | 2-24 mo |  |  | 0 | NR | NR | NR | NR | NR | NR |
| Htun, 2011{Htun, 2011 20 /id}  21273381  Germany  NR | clopidogrel LD 600 mg then 75 mg/d and aspirin 100  mg/d | LTA ADP | ischemic stroke | ischemic stroke | 1 year | low-responder group1 (K/DOQI index III-V)  N=165 | ischemic stroke | 2(1.2) | NR | NR | 0.08 (low responder vs responder) | NR | NR |  |
|  |  |  |  |  |  | responder group 1  (K/DOQI index III-V)  N=396 |  | 16 (4.1) |  |  |  |  |  |  |
|  |  |  |  |  |  | low-responder group 2  (K/DOQI index I-II)  N=161 |  | 1 (0.6) |  |  | 0.67 (low responder vs responder) |  |  |  |
|  |  |  |  |  |  | responder group 2  (K/DOQI index I-II)  N=613 |  | 6 (1.0) |  |  |  |  |  |  |
| Liu, 2011{Liu, 2011 12 /id}  21613806  China  None | Clopidogrel+aspirin | Aggregometry | Ischemic stroke | New focal neurologic deficit without bleeding on tomodensitoemtry confirmed by a neurologist to have occurred within the time frame (1 or 3 mo after PCI) | 1 month | Nonrespoders | 34 | 3 | OR (calculated)=16.1 | 0.8-321.2 | P=0.03 (nonresponder vs resp + low resp at 1month)  [Fishers exact] | NR |  |  |
|  |  |  |  |  |  | Low responders | 28 | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Responders | 44 | 0 |  |  | 0.38 across this and previous 2 rows (chi-square test) |  |  |  |
| Wang, 2009{Wang, 2009 130 /id}  19041120  China  NR | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | CVA | Cerebrovascular ischemia accident (CVA) | One year | Clopidogrel resistance | CVA | 2/65 (3.1) | OR=3.37 | 0.55-20.55 | 0.199 comparing with the following group | NO | NO |  |
|  |  |  |  |  |  | Normal response |  | 3/321  (0.9) |  |  |  |  |  |  |
| Gurbel, 2003{Gurbel, 2003 222 /id}  12796140  USA  NR | LD 300 mg clopidogrel and maintaining 75 mg daily | ADP-LTA | cerebrovascular  ischemic events | cerebrovascular  ischemic events | 30 days | Clopidogrel resistance | cerebrovascular  ischemic events | 0/50 | OR (calculated)=1.25 | NR | P=0.91 (nonresponder vs resp + low resp at 1month)  [Fishers exact] | NR | NO |  |
|  |  |  |  |  |  | Clopidogrel nonresistance |  | 0/63 |  |  |  |  |  |  |
| Ge, 2012{Ge, 2012 18184 /id}  21602258  China  NR | Clopidogrel 600 mg loading; maintenance clopidogrel 75 mg/d + aspirin 100 mg/d | LTA (ADP) | stroke | NR | 6 mo | Resistance (drop in reactivity <10% post-loading) | Stroke events | 0/65 (0%) | NA | NA | NR | NR | NR | NR |
|  |  |  |  |  |  | Non-resistance (drop ≥10% post-loading) |  | 0/287 (0%) |  |  |  |  |  |  |