Supporting Information

P2Y12 Polymorphisms and the Risk of Adverse Clinical Events in Patients Treated with Clopidogrel: a meta-analysis

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Supporting Material 1: Flow diagram of study selection

- Records identified through database searching (n=668)
- Additional records identified through other sources (n=0)

- Records after duplicates removed (n=458)

- Records screened (n=458)
  - Records excluded (n=434)
    - 238 irrelevant studies
    - 119 reviews
    - 59 studies without adverse events
    - 8 conference papers
    - 4 animal trials
    - 4 case reports
    - 2 non-English language study

- Full-text articles assessed for eligibility (n=24)
  - Full-text articles excluded (n=9)
    - 6 studies with incomplete data
    - 1 study with incorrect data
    - 1 study with follow-up <3 months
    - 1 study of non full-text

- Studies included in qualitative synthesis (n=15)

- Studies included in quantitative synthesis (meta-analysis) (n=14)

- Only has single genotype (n=1)
### Supporting Material 2: The characteristics of the included studies

<table>
<thead>
<tr>
<th>Author of study</th>
<th>Year</th>
<th>Country</th>
<th>Race</th>
<th>Studied Population</th>
<th>Treatment Protocol</th>
<th>Sample Size</th>
<th>Genetic locus</th>
<th>P-value for Hardy-Weinberg equilibrium</th>
<th>Follow-up (months)</th>
<th>Outcomes</th>
<th>NOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rudez G</td>
<td>2008</td>
<td>the Netherlands</td>
<td>Caucasian</td>
<td>patients treated with PCI</td>
<td>clopidogrel75mg/day plus aspirin 100mg/day</td>
<td>2062</td>
<td>rs2046934</td>
<td>&gt;0.05</td>
<td>9-12</td>
<td>TVR</td>
<td>5</td>
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<tr>
<td>Malek LA</td>
<td>2008</td>
<td>Poland</td>
<td>Caucasian</td>
<td>ACS treated with PCI</td>
<td>clopidogrel: LD 300 or 600 mg MD 75 mg/day aspirin: LD 300 mg MD 75 mg/day</td>
<td>105</td>
<td>rs2046934</td>
<td>&gt;0.05</td>
<td>12</td>
<td>nonfatal MI, cardiovascular death</td>
<td>7</td>
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<tr>
<td>Simon T</td>
<td>2009</td>
<td>France</td>
<td>Caucasian</td>
<td>acute MI</td>
<td>clopidogrel: LD 300 mg MD 75 mg/day aspirin: 100mg/day</td>
<td>2208</td>
<td>rs6809699 rs6785930</td>
<td>&gt;0.05</td>
<td>12</td>
<td>nonfatal MI, stroke, death</td>
<td>6</td>
</tr>
<tr>
<td>Tang XF</td>
<td>2013</td>
<td>China</td>
<td>Han Chinese</td>
<td>ACS treated with PCI</td>
<td>clopidogrel: LD 300 mg MD 75 mg/day aspirin: LD 300 mg MD 100 mg/day</td>
<td>577</td>
<td>rs6785930</td>
<td>&gt;0.05</td>
<td>12</td>
<td>cardiovascular death, nonfatal MI, unplanned TVR, ST, bleeding</td>
<td>7</td>
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<tr>
<td>Viviani Anselmi C</td>
<td>2013</td>
<td>Italy</td>
<td>Caucasian</td>
<td>stable CAD treated with DES implantation</td>
<td>clopidogrel:75mg/day aspirin:100mg/day</td>
<td>1432</td>
<td>rs2046934</td>
<td>0.72</td>
<td>12</td>
<td>cardiac death, nonfatal MI, ST</td>
<td>7</td>
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<tr>
<td>Lin YJ</td>
<td>2014</td>
<td>China</td>
<td>Han</td>
<td>patients</td>
<td>clopidogrel:75mg/day</td>
<td>90</td>
<td>rs6809699</td>
<td>&gt;0.05</td>
<td>12</td>
<td>in-stent restenosis</td>
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<tr>
<td>Study</td>
<td>Year</td>
<td>Country</td>
<td>Ethnicity</td>
<td>Condition</td>
<td>Treatments</td>
<td>Genotypes</td>
<td>Events</td>
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<td>Sun B</td>
<td>2015</td>
<td>China</td>
<td>Han Chinese</td>
<td>CAD treated with PCI</td>
<td>aspirin: LD 300 mg MD 100 mg/day ; clopidogrel: LD 300 mg MD 75 mg/day aspirin:100 mg/day</td>
<td>rs6785930</td>
<td>in-stent restenosis, unstable angina pectoris requiring hospitalization, acute MI, stroke, death</td>
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<tr>
<td>Zhang JH</td>
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<td>China</td>
<td>Han Chinese</td>
<td>STEMI treated with PCI</td>
<td>aspirin:100 mg/day</td>
<td>rs6809699 rs6785930</td>
<td>cardiovascular death, nonfatal MI, unplanned TVR, ST, bleeding events</td>
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<tr>
<td>Li XQ</td>
<td>2016</td>
<td>China</td>
<td>Han Chinese</td>
<td>IS underwent stenting</td>
<td>aspirin:100 mg/day</td>
<td>rs2046934 0.121</td>
<td>TIA, IS, MI, vascular-related mortality</td>
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<td>Siasos G</td>
<td>2016</td>
<td>Greece</td>
<td>Caucasian</td>
<td>stable CAD</td>
<td>aspirin:75mg/day</td>
<td>rs6785930</td>
<td>cardiovascular death, nonfatal MI, urgent TVR, nonfatal stroke</td>
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<td>Ou W</td>
<td>2016</td>
<td>China</td>
<td>Han Chinese</td>
<td>coronary heart disease</td>
<td>aspirin:75mg/day ; clopidogrel: MD 75 mg/day aspirin glycoprotein IIb/IIIa inhibitor</td>
<td>rs2046934 rs6809699 rs6785930</td>
<td>recurrent angina, recurrent MI, ST, stent restenosis, cardiac death</td>
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<td>Yang HH</td>
<td>2016</td>
<td>China</td>
<td>Han Chinese</td>
<td>Coronary heart disease</td>
<td>aspirin:100 mg/day</td>
<td>rs2046934 &gt;0.05</td>
<td>cardiac death, nonfatal MI, unstable angina, TVR</td>
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<td></td>
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<tr>
<td>Authors</td>
<td>Year</td>
<td>Country</td>
<td>Ethnicity</td>
<td>Study Population</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>SNPs</td>
<td>p-Value</td>
<td>Follow-up</td>
<td>Outcomes</td>
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<tr>
<td>Wang XD</td>
<td>2016</td>
<td>China</td>
<td>Han Chinese</td>
<td>Patients treated with PCI</td>
<td>LD 300 mg MD 100 mg/day clopidogrel: LD 600 mg MD 75 mg/day aspirin: LD 300 mg MD 100 mg/day</td>
<td>336</td>
<td>rs2046934</td>
<td>&gt;0.05</td>
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<td>Cardiac death, unstable angina pectoris, nonfatal MI, TLR, cerebral ischemia, TIA, AHF, bleeding</td>
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<tr>
<td>Li MN</td>
<td>2017</td>
<td>China</td>
<td>Han Chinese</td>
<td>ACS treated with PCI</td>
<td>clopidogrel: LD 300 mg MD 75 mg/day aspirin: 100 mg/day</td>
<td>498</td>
<td>rs6809699 rs6785930</td>
<td>&gt;0.05</td>
<td>3-12</td>
<td>Recurrent angina, acute MI, emergency revascularization, in-stent restenosis, ST, mortality</td>
<td></td>
</tr>
</tbody>
</table>

Supporting Material 3: Funnel plot of meta-analysis of the P2Y12 polymorphism and ischemic events. A: T744C, CC+CT vs TT, B: T744C, CC vs TT+CT. C: G52T, TT+TG vs GG, D: G52T, TT vs GG+TG. E: C34T, TT+TC vs CC, F: C34T, TT vs CC+TC