PCI-CLARITY: Effect of clopidogrel (PLAVIX) pre-treatment before PCI in patients with STEMI treated with fibrinolitics

**BOTTOM LINE**
In PCI-CLARITY, patients with STEMI treated with fibrinolitics and DAPT (ASA + clopidogrel), vs ASA alone, before PCI had:
- ↓ risk of CV death, recurrent MI or stroke for 30 days after PCI (NNT=39); individual components did not reach significance
- no difference in major or minor bleeding risk (NS)

**BACKGROUND**
- The CLARITY TIMI 28 study assessed the efficacy & safety of adding DAPT (ASA + clopidogrel) vs ASA alone to fibrinolytic therapy in individuals with STEMI.
- The PCI-CLARITY study was a prospectively designed sub-study of the CLARITY TIMI 28 trial for individuals who underwent PCI.
- At the time of publication, DAPT before and after PCI was not standard of practice; however, these are considered landmark trials which helped shape our current approach.
- Current clinical practice guidelines recommend DAPT with ASA and a P2Y12 inhibitor (clopidogrel, prasugrel or ticagrelor) for 12 months after STEMI with PCI, followed by ASA indefinitely.

**SECONDARY ENDPOINTS from randomization to 30 days (mean 33 days)**
- CV death or MI: 7.2% vs 6.1%, p=0.62; NNT=39
- CV death, recurrent MI, stroke: 4.5% vs 3.9%, p=0.62; NNT=39

**SECONDARY ENDPOINTS from PCI to 30 days after randomization**
- CV death, recurrent MI, stroke: 3.6% vs 2.2%, p=0.62; NNT=39
- MI: 4.2% vs 2.1%, p=0.62; NNT=39

**PRIMARY ENDPOINTS**
- CV death, recurrent MI, stroke: 3.6% vs 2.2%, p=0.62; NNT=39

**TRIAL BACKGROUND**
- PCI-CLARITY: PCI was performed at the discretion of the local investigator. ITT for efficacy & per protocol for safety outcomes.
- INTERVENTION: in addition to a fibrinolytic (~e heparin) & ASA (150-325mg on the first day, then 75-162mg daily thereafter):
  - Pre-PCI: randomized, double-blind clopidogrel 300mg LD then 75mg daily or placebo until angiography (CLARITY)
  - Post-PCI: all stented patients (95%) received open-label clopidogrel 300mg LD (~75%) then 75mg daily (~90%) (PCI-CLARITY)
- INCLUSION: CLARITY: age 18 to 75 years, onset of ischemic discomfort <12 hr before randomization (last or more than 20 minutes), ST elevation at least 0.1 mV in at least 2 contiguous limb leads or at least 0.2 mV in at least 2 contiguous precordial leads, or left bundle branch block, planned treatment with fibrinolytic, anticoagulant (if receiving a fibrin-specific lytic) and aspirin.
- PCI-CLARITY: Met enrolment criteria for CLARITY and underwent PCI during index hospitalization.
- EXCLUSION: CLARITY: treatment with clopidogrel within 7 days prior to enrolment, or clopidogrel or glycoprotein IIb/IIIa inhibitor before angiography was planned, CI to fibrinolitics, cardiogenic shock, intention of angiography within 48 hours in absence of new clinical indication, undergone prior CABG, ≤67 kg who received >4000 unit bolus of heparin or >67 kg who received > 5000 unit bolus of heparin or received greater than standard doses of LMWH. Excluded after randomization if did not get fibrinolytic drug, underwent CABG, received medical therapy, or did not have PCI on index hospitalization.
- POPULATION at baseline: n=1,863 of 3,491 (53.4% from CLARITY)
  - Mean age ~57 yrs 28% between 65-75 yr, ~82% Caucasian, # of patients from North America not reported
  - 50.3% smoker, 41% HTN, 40% hyperlipidemia, anterior MI 38.9%, 15.4% DM, prior MI 8.3%, prior PCI 5.5%
  - Fibrinolytic: median 2.35 hr from symptom onset to fibrinolytic, 79% fibrin-specific 98.5% received heparin, 21% non-fibrin-specific
  - PCI: median 3 days from randomization to PCI. 32 days clopidogrel vs. 29.9 days placebo, p=0.003; infarct related artery patency: 84% before PCI; 86.9% clopidogrel vs. 80.8% placebo, p<0.001, 98.7% after PCI; ~32% glycoprotein IIb/IIIa; 95% coronary artery stenting; open-label clopidogrel: 77.6% LD at time of PCI, 89.6% MD given after PCI.

**RESULTS**

**TABLE: EFFICACY ENDPOINTS (SAFETY ENDPOINTS DISCUSSED IN COMMENTS)**

<table>
<thead>
<tr>
<th>PRIMARY ENDPOINTS from PCI to 30 days after randomization</th>
<th>Clopidogrel LD 300-600mg daily</th>
<th>Placebo n=930</th>
<th>ARR</th>
<th>OR 95% CI</th>
<th>NNT</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, recurrent MI, stroke</td>
<td>3.6%</td>
<td>6.2%</td>
<td>2.6%</td>
<td>0.54 (0.35-0.85)</td>
<td>39 / 30 days</td>
<td>None of individual components for the primary composite endpoint reached statistical significance.</td>
</tr>
<tr>
<td>SECONARY ENDPOINTS from PCI to 30 days after randomization</td>
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</tr>
<tr>
<td>CV death or MI</td>
<td>3.3%</td>
<td>5.4%</td>
<td>2.1%</td>
<td>0.58 (0.36-0.94)</td>
<td>48 / 30 days</td>
<td>~2/3 of all MIs occurred before PCI.</td>
</tr>
<tr>
<td>CV death</td>
<td>1.4%</td>
<td>2.6%</td>
<td>NS</td>
<td>0.49 (0.24-1.03)</td>
<td>-</td>
<td>Kaplan Meier curve separated after the first day of therapy, and continued to diverge over time.</td>
</tr>
<tr>
<td>Recurrent MI</td>
<td>1.9%</td>
<td>3.1%</td>
<td>NS</td>
<td>0.60 (0.33-1.11)</td>
<td>-</td>
<td>LD: all patients received clopidogrel 300mg at study entry. ~75% received another 300mg at time of PCI.</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.4%</td>
<td>1.2%</td>
<td>NS</td>
<td>0.35 (0.11-1.11)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>SECONDARY ENDPOINTS before PCI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent MI, stroke</td>
<td>4%</td>
<td>6.2%</td>
<td>2.2%</td>
<td>0.62 (0.4-0.95)</td>
<td>46 / 3 days</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>4%</td>
<td>6.1%</td>
<td>2.1%</td>
<td>0.6 (0.38-0.95)</td>
<td>47 / 3 days</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>0%</td>
<td>0.1%</td>
<td>NS</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>SECONDARY ENDPOINTS from randomization to 30 days (mean 33 days)</td>
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</tr>
<tr>
<td>CV death, recurrent MI, stroke</td>
<td>7.5%</td>
<td>12%</td>
<td>4.5%</td>
<td>0.59 (0.43-0.81)</td>
<td>23 / 33 days</td>
<td></td>
</tr>
<tr>
<td>CV death or MI</td>
<td>7.2%</td>
<td>11.1%</td>
<td>3.9%</td>
<td>0.62 (0.45-0.86)</td>
<td>26 / 33 days</td>
<td></td>
</tr>
<tr>
<td>CV death</td>
<td>1.4%</td>
<td>2.6%</td>
<td>NS</td>
<td>0.49 (0.24-1.03)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Recurrent MI</td>
<td>5.9%</td>
<td>8.9%</td>
<td>3%</td>
<td>0.64 (0.44-0.92)</td>
<td>34 / 33 days</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>0.4%</td>
<td>1.3%</td>
<td>NS</td>
<td>0.32 (0.1-1.01)</td>
<td>-</td>
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</tbody>
</table>
### STRENGTHS, LIMITATIONS, & UNCERTAINTIES

**STRENGTHS:**
- Important clinical endpoints (e.g. cardiovascular death, MI) with blinded adjudication of outcomes.
- All patients enrolled in the study were accounted for (1 lost to follow up on treatment arm after 10 d included in primary analysis).
- Used a propensity score to minimize potential selection bias due to non-randomized PCI.

**LIMITATIONS:**
- Short follow up period of only 30 days (followed up with a telephone call and then confirmed using medical records).
- Power calculated for CLARITY and not for PCI-CLARITY.
- Narrow population studied (only STEMI treated with fibrinolytics e.g. tenecteplase ~47%, streptokinase ~30%).
- Patients >75 years old were excluded from the trial.
- Did not report PPI use or stent thrombosis

**UNCERTAINTIES:**
- Optimal length of DAPT after PCI.
- How much of the benefit was due to the pre-PCI loading dose, versus 30 days of open-label clopidogrel.

### RxFiles RELATED LINKS
- Duration of DAPT & Triple Therapy RxFiles Chart

### ACKNOWLEDGEMENTS
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### References