Single Antiplatelet Regimen after DES: already an Option?

Marco Valgimigli, MD, PhD
University Hospital of Bern, Switzerland

COI: Research grants from Astra Zeneca to ECRI and to Erasmus for the conduct of Global Leaders and Hi-Tech

a Dual therapy with oral anticoagulation and clopidogrel may be considered in selected patients (low ischaemic risk).

b Aspirin as an alternative to clopidogrel may be considered in patients on dual therapy (i.e., oral anticoagulation plus single antiplatelet); triple therapy may be considered up to 12 months in patients at very high risk for ischaemic events.

c Dual therapy with oral anticoagulation and an antiplatelet agent (aspirin or clopidogrel) beyond one year may be considered in patients at very high risk of coronary events. In patients undergoing coronary stenting, dual antiplatelet therapy may be an alternative to triple or dual therapy if the CHA2DS2-VASc score is 1 (males) or 2 (females).
## WOEST Trial

### Secondary Endpoints

**Cumulative incidence of bleeding**

- **Triple therapy group**
  - Days 0-30: 44.9%
  - Days 30-60: 19.5%

- **Double therapy group**
  - Days 0-30: 2.6%
  - Days 30-60: 3.3%

**RRR: 64%**

**NNH: 4**

<table>
<thead>
<tr>
<th>Event</th>
<th>Double therapy group</th>
<th>Triple therapy group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2.6</td>
<td>6.4</td>
<td>0.027</td>
</tr>
<tr>
<td>MI</td>
<td>3.3</td>
<td>4.7</td>
<td>0.382</td>
</tr>
<tr>
<td>TVR</td>
<td>1.1</td>
<td>6.8</td>
<td>0.128</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.5</td>
<td>2.9</td>
<td>0.165</td>
</tr>
<tr>
<td>ST</td>
<td>1.5</td>
<td>3.2</td>
<td></td>
</tr>
</tbody>
</table>

**WOEST Trial**
How about patents who do not need OAC?
Coronary stent implantation

Aspirin P2Y12i

30 days 60 days 90 days 180 days ≥360 days …

All-comers PCI population
(ACS and Stable CAD patients)
(N = 16,000)

Experimental Treatment Strategy
Bivalirudin*-supported BioMatrix family stent implantation
1:1 Randomization, Open-Label Design

Reference Treatment Strategy

Is Aspirin a still contemporary treatment option?
Is less more?

Primary Endpoint (Effectiveness): Death or Q wave MI
DSMB has not stopped the study!!

Enrolment
18 Participating Countries

14 European countries:
- Germany: 17 sites, 2278 patients
- Belgium: 6 sites, 2189 patients
- United Kingdom: 18 sites, 1720 patients
- Italy: 6 sites, 1578 patients
- Poland: 7 sites, 1540 patients
- The Netherlands: 9 sites, 1164 patients
- Spain: 9 sites, 952 patients
- Bulgaria: 8 sites, 944 patients
- France: 13 sites, 851 patients
- Switzerland: 6 sites, 706 patients
- Austria: 5 sites, 672 patients
- Hungary: 8 sites, 527 patients
- Denmark: 2 sites, 131 patients
- Portugal: 4 sites, 112 patients

4 non-EU countries:
- Brazil: 5 sites, 248 patients
- Canada: 2 sites, 170 patients
- Singapore: 2 sites, 142 patients
- Australia: 4 sites, 83 patients

The ranking is based on amount of patients / amount of active sites

<table>
<thead>
<tr>
<th>Country</th>
<th>Sites</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>6</td>
<td>2189</td>
</tr>
<tr>
<td>Italy</td>
<td>6</td>
<td>1578</td>
</tr>
<tr>
<td>Poland</td>
<td>7</td>
<td>1540</td>
</tr>
<tr>
<td>Spain</td>
<td>9</td>
<td>952</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>8</td>
<td>944</td>
</tr>
<tr>
<td>France</td>
<td>13</td>
<td>851</td>
</tr>
<tr>
<td>Switzerland</td>
<td>6</td>
<td>706</td>
</tr>
<tr>
<td>Austria</td>
<td>5</td>
<td>672</td>
</tr>
<tr>
<td>Hungary</td>
<td>8</td>
<td>527</td>
</tr>
<tr>
<td>Denmark</td>
<td>2</td>
<td>131</td>
</tr>
<tr>
<td>Portugal</td>
<td>4</td>
<td>112</td>
</tr>
</tbody>
</table>

1. **Belgium**
   - 365 pts/site
   - 6 active sites

2. **Italy**
   - 262 pts/site
   - 6 active sites

3. **Poland**
   - 219 pts/site
   - 7 active sites
“Less is more”: Aspirin withdrawal

Post-PCI:
GLOBAL LEADERS (NCT01813435) started on February 2013 (ticagrelor)
TWILIGHT (NCT02270242) started on August 2015 (ticagrelor)
TICO (NCT02494895) started on July 2015 (ticagrelor)

ACS patients:
GEMINI-ACS-1 (NCT02293395) started on April 2015 (rivaroxaban)

Post-ACS:
COMPASS (NCT01776424) started on February 2014 (rivaroxaban)

Post-PCI in AF patients:
PIONEER AF-PCI (NCT01830543) started on May 2013 (rivaroxaban)
REDUAL-PCI (NCT02164864) started on July 2014 (dabigatran)
AUGUSTUS (NCT02415400) started on June 2015 (apixaban)
ENTRUST AF-PCI going to be registered (edoxaban)

Post-TAVI:
GALILEO (NCT02556203) started on December 2015 (rivaroxaban)
ATLANTIS (NCT02664649) started on February 2016 (apixaban)
A blinded trial at 56 North American centers that compared the effects of ticlopidine hydrochloride (500 mg daily) with those of aspirin (1300 mg daily) on the risk of stroke or death. The medications were randomly assigned to 3069 patients with recent transient or mild persistent focal cerebral or retinal ischemia. Follow-up lasted for two to six years.
CAPRIE

19,185 pts; recent stroke, recent MI or PAD

ASA: 325 mg/d; Clopidogrel 75 mg/d

RRR 9.4%

1° EP: Vascular death, MI or stroke
MATCH study

7,599 pts with recent stroke or TIA. All on clopidogrel. Randomization to receive ASA or Placebo on top.

Vascular death, stroke, MI, rehosp for ACS

Intracranial bleeding

Lancet 2004; 364: 331–37
SOCRATES

Trial design: Patients with acute ischemic stroke or TIA were randomized in a 1:1 fashion to receive either ticagrelor 180 mg load + 90 mg BID or aspirin 300 mg load + 100 mg/day within 24 hours of presentation. They were followed for 3 months.

Results

- Primary outcome, death, MI or stroke, for ticagrelor vs. aspirin: 6.7% vs. 7.5%, HR = 0.89, 95% CI 0.78-1.01, p = 0.07
- Death: 1.0% vs. 0.9%, p = 0.36; All strokes: 5.9% vs. 6.8%, p = 0.03; ischemic stroke: 5.8% vs. 6.7%, p = 0.046
- Major bleeding: 0.5% vs. 0.6%, p = 0.45; intracranial hemorrhage: 0.2% vs. 0.3%, p = 0.3

Conclusions

- Ticagrelor monotherapy was not superior to aspirin in reducing cardiovascular events in patients with low-acuity ischemic stroke or high-risk TIA
- Major bleeding was similar
- Unknown if a benefit may be observed on longer duration of follow-up, or in patients with proven ischemic stroke only

Conclusive Remarks

- It is too early to drop aspirin, the oldest drug still part of our unavoidable anti-thrombotic armamentarium after DES in patients not needing OAC.

- This question is being asked.

- The Global leaders is the first major study asking this question but a conclusive answer will require consistent evidence coming from multiple RCTs.

"having to choose between two evils"