TRILOGY-ACS: Prasugrel versus clopidodrel for patients with Unstable Angina/NSTEMI who are medically managed without revascularization.

Discussant
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August 26, 2012 – 11:55-12:00
Raffaele De Caterina –
Disclosures related to this study

- Speaker fees and honoraria from
  - Lilly-Daiichi Sankyo
  - Astra-Zeneca
  - Bayer
TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medically manage Acute Coronary Syndromes (TRILOGY-ACS) Trial

Why needed?

- Despite recommendations for moderate/high risk patients with NSTE-ACS, about half of them do not undergo early revascularization.
- Such medically-treated pts usually have more comorbidities, a higher risk of bleeding, and a worse global outcome than invasively treated patients, and here the benefit-risk balance changing clopidogrel with a more potent platelet inhibitor is uncertain.
- TRITON-TIMI 38, with prasugrel vs clopidogrel on top of aspirin in ACS – both STEMI and NSTE-ACS – was conducted in a population of invasively treated patients.
- There was a prohibitively high risk of bleeding in TRITON-TIMI 38 for patients ≥75 years of age – therefore the assessment of a lower-dose regimen for prasugrel in these patients was warranted.
TRILOGY-ACS - Strengths

- Randomized, double-blind, double-dummy, active-control, event-driven trial, with sample size (n=9326) and follow-up (median >14 months) adequate to detect a clinically significance difference (22% RRR in the primary outcome)
- Risk features of the study population: NSTEMI or unstable angina (UA) with >1 mm of ST depression plus 1 of 4 additional risk criteria: age ≥60 years, diabetes, prior MI, prior revascularization (PCI or CABG).
- Good geographical diversity (33.1% of patients from Central/Eastern Europe)
- Long follow-up (>14 months median)
TRILOGY-ACS – Strengths (con’t)

- 22.3% of pts ≥ 75 years of age
- Prasugrel maintenance dose was adjusted to 5 mg for those ≥75 years (never previously tested here) and in pts <60 kg of body weight
Results

- Primary efficacy endpoint (CV death, MI and stroke in pts <75 years): not statistically different
- Similar results for other efficacy endpoint including CV death; MI; stroke; all-cause death; CV death+MI; recurrent hospitalization for UA; All-cause death, MI or stroke; Net clinical benefit
  - Therefore: Results not supporting the trial main hypothesis
- None of the safety (mostly bleeding endpoint) was statistically different between the two arms, including pts >75 (here indicating the successful adoption of the modified regimen), but numerically higher in the prasugrel group for moderate/minor bleeding.
- Separation of the curves after 12 months
Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management: substudy from prospective randomised PLATElet inhibition and patient Outcomes (PLATO) trial
Novel P2Y12 angagonists vs clopidogrel in medically treated ACS – Main Results

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<th>PLATO Substudy*</th>
<th>TRILOGY-ACS**</th>
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<tr>
<td><strong>Primary endpoint</strong></td>
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<tr>
<td>Vascular death, MI</td>
<td>0.85 (0.73 to 1.00)</td>
<td>0.91 ((0.79-1.05)</td>
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<td>and stroke</td>
<td>0.045</td>
<td>0.21</td>
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<tr>
<td>CV death, MI and</td>
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<td>stroke in pts &lt;75</td>
<td>0.96 (0.86-1.07)</td>
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<td>years</td>
<td>0.45</td>
<td>0.40</td>
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<td><strong>All cause death</strong></td>
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<td>HR (95% CI)</td>
<td>0.75 (0.61 to 0.93)</td>
<td>0.94 (0.82-1.08)</td>
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<td>0.010</td>
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** Roe MT et al. NEJM 2012
ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Recommendations for oral antiplatelet agents

**Ticagrelor** (180-mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g., elevated troponins), regardless of initial treatment strategy, and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced).

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>Ticagrelor</td>
<td>I</td>
<td>B</td>
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<tr>
<td>Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for <strong>P2Y_12</strong>-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.</td>
<td>I</td>
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