ESC Congress 2012

Munich, Germany – August 25-29, 2012

Hot Line

HOT LINE I: Late Breaking Trials on Prevention to Heart Failure

August 26, 2012 – 11:00-12:30

Room Munich – Central Village

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

Discussant

Raffaele De Caterina

"G. d'Annunzio" University – Chieti and
"G. Monasterio" Foundation – Pisa, Italy

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

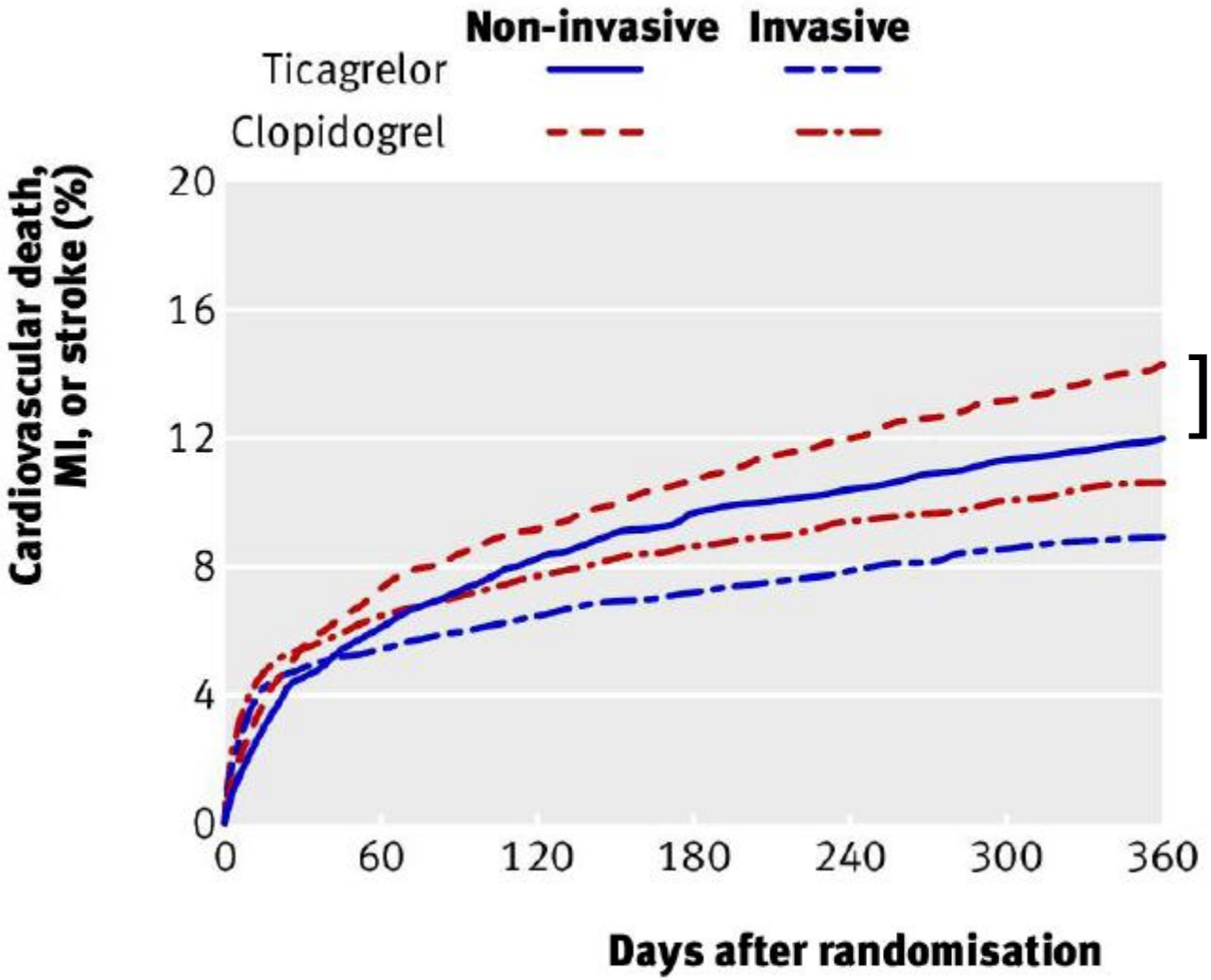
Results

- 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

BMJ

BMJ 2011;342:d3527 doi: 10.1136/bmj.d3527



Non-invasive

Novel P2Y12 angagonists vs clopidogrel in medically treated ACS – Main Results

	PLATO Substudy*	TRILOGY-ACS**
Primary endpoint	**Vascular death, MI and stroke**	**CV death, MI and stroke in pts <75 years**
HR (95% CI)	**0.85 (0.73 to 1.00)**	**0.91 ((0.79-1.05)**
P	**0.045**	**0.21**
Vascular death, MI and stroke		
HR (95% CI)	**0.85 (0.73 to 1.00)**	**0.96 (0.86-1.07)**
P	**0.045**	**0.45**
All cause death		
HR (95% CI)	**0.75 (0.61 to 0.93)**	**0.94 (0.82-1.08)**
P	**0.010**	**0.40**

*James SK et al. BMJ 2011;342:d3527 doi: 10.1136/bmj.d3527

** Roe MT et al. NEJM 2012

European Heart Journal (2011) **32**, 2999–3054
doi:10.1093/eurheartj/ehr236

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).	I	B
Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for $P2Y_{12}$-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.[d]	I	B