Probufol for prevention of cardiovascular events in ischemic stroke patients with high risk of cerebral hemorrhage (PICASSO) study: a multicenter, randomized controlled trial

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On behalf of PICASSO investigators

3rd European Stroke Organisation Conference, Prague, Czech Republic
Lipid-lowering non-statin, Probucol

- **Cholesterol-lowering effect**
  1) increasing LDL cholesterol catabolism,
  2) inhibiting cholesterol synthesis,
  3) delaying cholesterol absorption,
  4) inhibiting LDL cholesterol oxidation.

  - CETP (cholesterylester transfer protein) “activator”

- **Other pleiotropic effects**
  1) decreasing inflammation,
  2) improving endothelial function,
  3) preventing blood-brain barrier dysfunction.
**PICASSO design**

**Aim**
- To test the efficacy of probucol, non-statin lipid-lowering agent, in addition to standard lipid regimen in ischemic stroke patients with high risk of cerebral hemorrhage

**Inclusion**
- patients with onset of TIA or ischemic stroke within 180 days prior to screening
- adults older than 20 years
- patients with high risk of hemorrhagic stroke by any of:
  1) history of ICH, 2) ICH sequelae on GRE (≥ 8 mm), and 3) multiple microbleeds

**Design**
- 70 centers in three countries (South Korea, Hong Kong, Philippines)
- Two x two factorial design:
  Probucol arm (probucol vs. non-probucol)
  Antiplatelet arm (aspirin vs. cilostazol)
- Open-label, blinded-endpoint trial: oral probucol (250 mg twice) vs. none
- Superiority testing for the primary efficacy endpoint*
  * a composite of stroke, myocardial infarction, or vascular death

*ClinicalTrials.gov (NCT01013532); Int J Stroke, 2015*
HR 0.69 (95% CI, 0.50–0.97), p = 0.031

Primary endpoint: stroke, MI, or cardiovascular death

Number at risk

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<th>Group</th>
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<th>3</th>
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<td>583</td>
<td>390</td>
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<tr>
<td>Non-probucol</td>
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<td>578</td>
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