# Probucol 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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# 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**

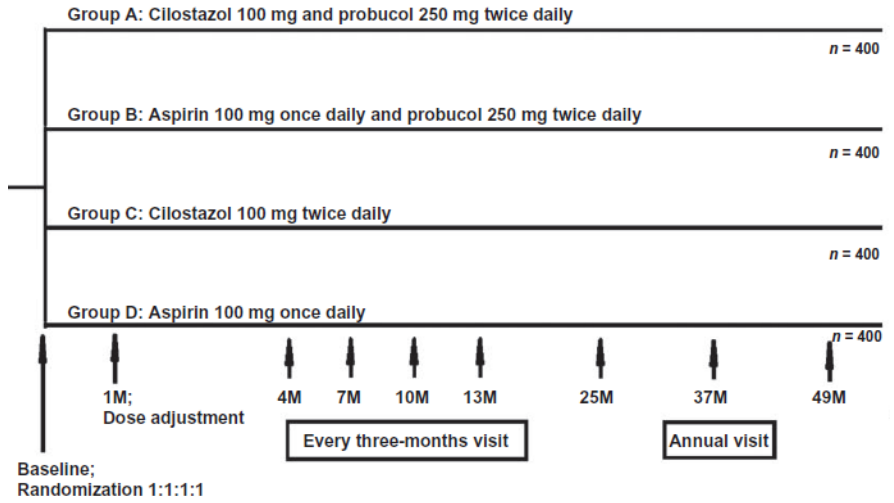
  - To test the efficacy of probucol, non-statin lipid-lowering agent, in addition to standard lipid regimen in ischemic stroke patients with high risk of cerebral hemorrhage

- **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

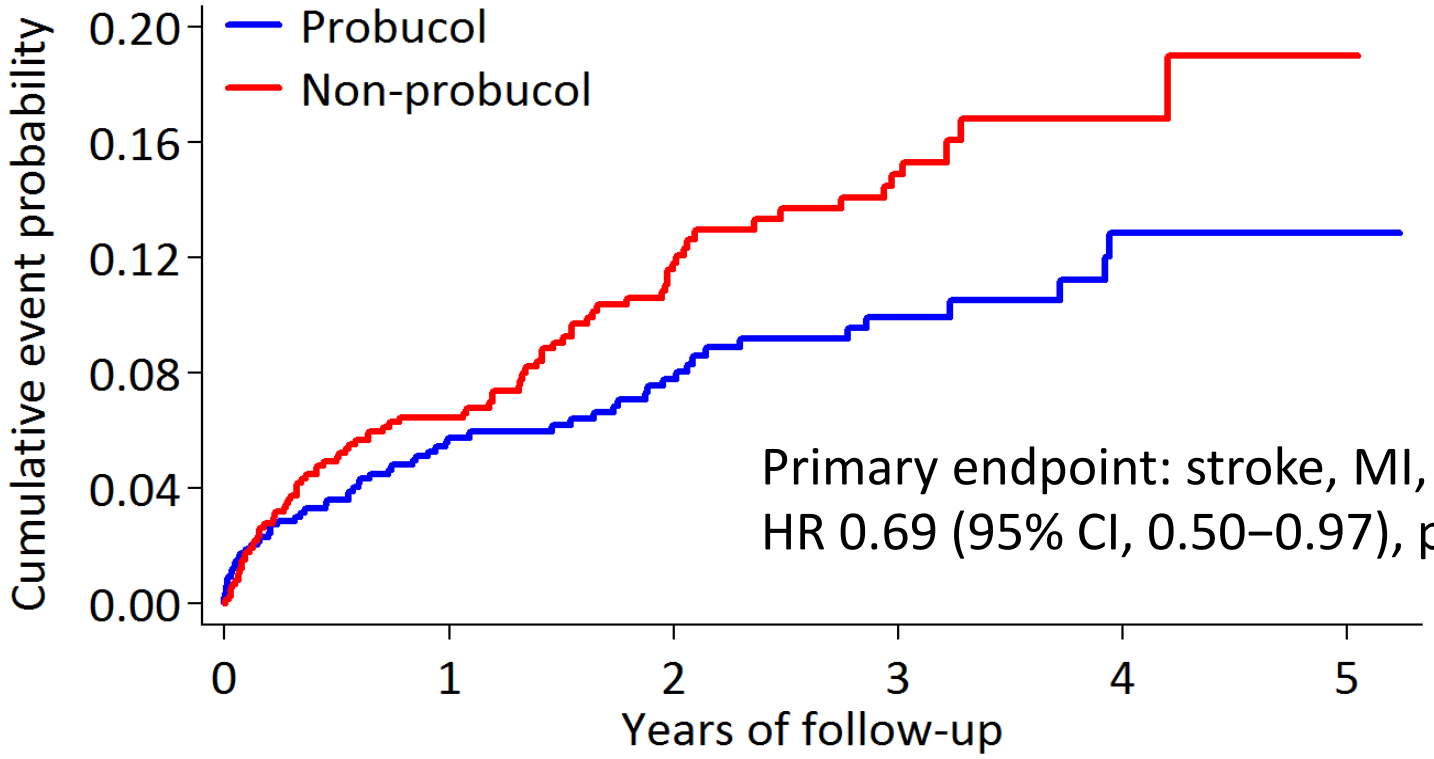
- **Design**

  - 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*

# PICASSO primary endpoint




Primary endpoint: stroke, MI, or cardiovascular death
HR 0.69 (95% CI, 0.50–0.97), p = 0.031

| Number at risk | | | | | | |
|---|---|---|---|---|---|---|
| Probucol | 756 | 583 | 390 | 244 | 107 | 15 |
| Non-probucol | 756 | 578 | 352 | 208 | 79 | 9 |