PANTHER

P2Y12 inhibitor versus aspirin monotherapy in patients with coronary artery disease – Discussion

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August 29, 2022

Declaration of interest

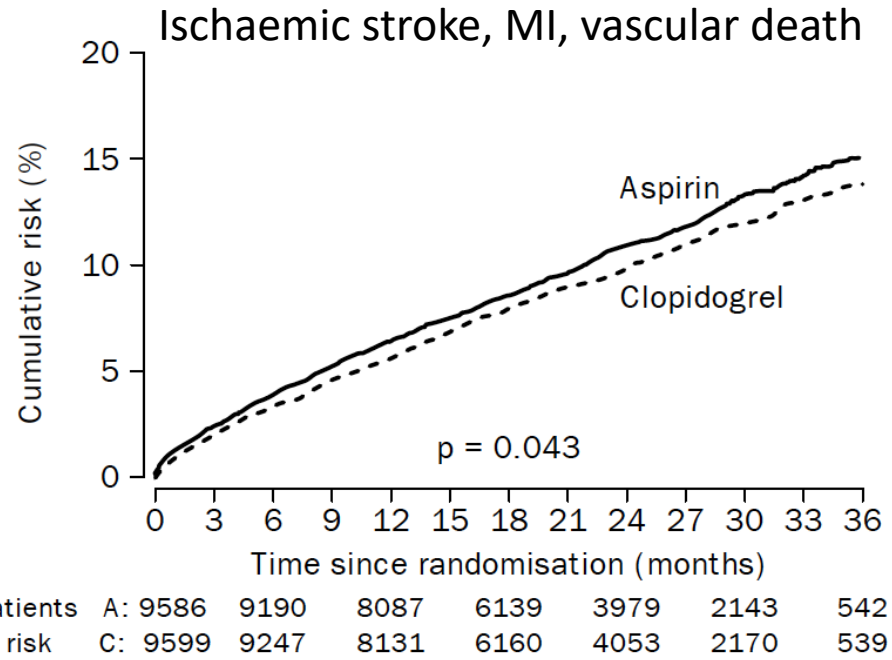
- I have nothing to declare

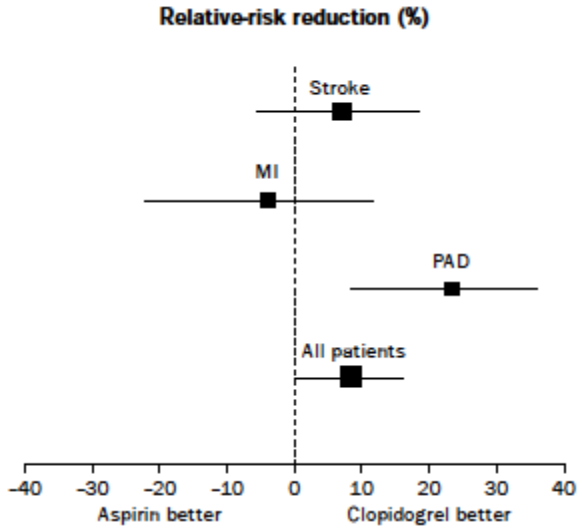
PANTHER

- **ASA monotherapy is first line for secondary prevention in CCS patients without an indication for OAC and/or DAPT (I, A)**
- **Monotherapy with P2Y12 inhibitors may be considered in patients with PAD or cerebrovascular disease (IIb, B)**

Knuuti et al., 2019 ESC Guidelines, Eur Heart J. 2020

Historic evidence from the CAPRIE trial





Benefit of clopidogrel in patients with PAD

CAPRIE Steering Committee, Lancet 1996

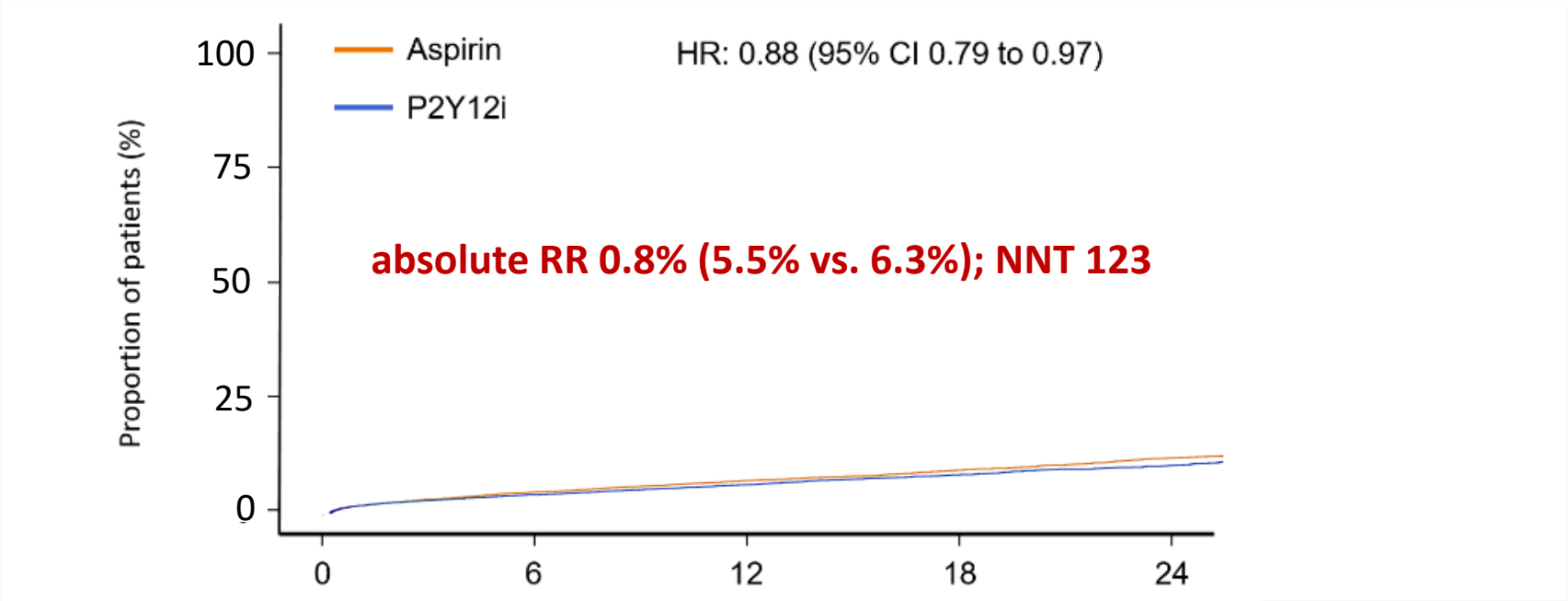
PANTHER – key features of trials included

Trial acronym	Date of publication	Number of patients*	Rate of revascularization (%)*	Type of revascularization	Type of P2Y12 inhibitor
CAPRIE	1996	19,185	-	-	Clopidogrel
CADET	2004	184	-	-	Clopidogrel
ASCET	2012	1,001	91.5	PCI / CABG	Clopidogrel
DACAB	2018	500	100	CABG	Ticagrelor
GLASSY	**2019**	**7,585**	**100**	**PCI**	**Ticagrelor**
TICAB	**2019**	**1,859**	**100**	**CABG**	**Ticagrelor**
HOST-EXAM	**2021**	**5,438**	**100**	**PCI**	**Clopidogrel**

***Numbers refer to entire trial (overall population of PANTHER)**

Key findings of PANTHER

CV death, MI or stroke



Valgimigli M et al., ESC 2022

PANTHER – Strengths

- PANTHER is a well-performed contemporary meta-analysis conducted by an experienced team of researchers.
- The findings have important clinical implications.
- In contrast to previous analyses, PANTHER is an individual participant data meta-analysis.
- PANTHER only enrolled patients with documented CAD.
- Ticlopidine did not contribute to the study results.

PANTHER – Open questions

- **CAPRIE had a high relative weight in PANTHER**
- **Approx. 10,000 patients were enrolled prior to 2018**
  - →Applicability to patients receiving contemporary therapy
  - →Yet, contribution of modern management greater than in previous analyses
- **Substantial subgroup (≈7,000 patients) without revascularization**
  - →Anti-ischemic advantage of P2Y12 inhibition derived from revascularization

PANTHER – Open questions

- **The mean patient age was 64 years**

  →Applicability to older patients is unclear (subgroup analysis)

- **Previous bleeding history was low (0.4%) in PANTHER**

  →Potential bias for low bleeding risk patients (e.g. HOST-EXAM)

- **Adherence rates tend to favour ASA compared to ticagrelor**

- **Prasugrel was not used in PANTHER**

  →Results may not be generalized to all P2Y12 inhibitors

- **Low effect size and no effect on mortality**

  →NNT of 123 needs to be weighed against cost effectiveness

Personal conclusion – is it time to switch standards?

- PANTHER is an important study evaluating the dogma of ASA as first choice in antiplatelet management of CCS patients
- ASA is a valid standard, as it is associated with less non-compliance and fewer off-target side-effects (compared with ticagrelor), less variation in treatment response (compared with clopidogrel), and most likely is more cost-effective given the low effect size of P2Y12 inhibitors.
- Yet, based on PANTHER and also HOST-EXAM, it is reasonable to use P2Y12 inhibitors instead of ASA monotherapy in younger CCS patients with a history of revascularization that have a low bleeding risk or a high risk of gastrointestinal bleeding.