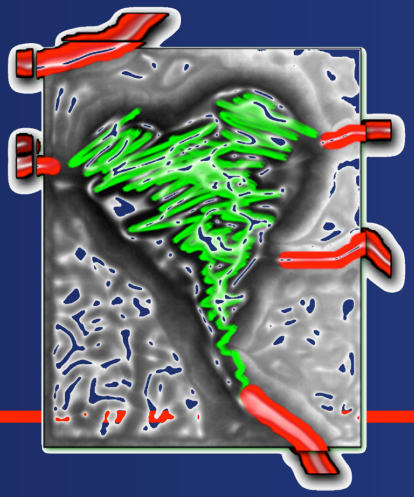

Single Antiplatelet Regimen after DES: already an Option ?

Marco Valgimigli, MD, PhD
University Hospital of Bern, Switzerland

COI: Research grants from Astra Zeneca to ECRI and to Erasmus for the conduct of Global Leaders and Hi-Tech

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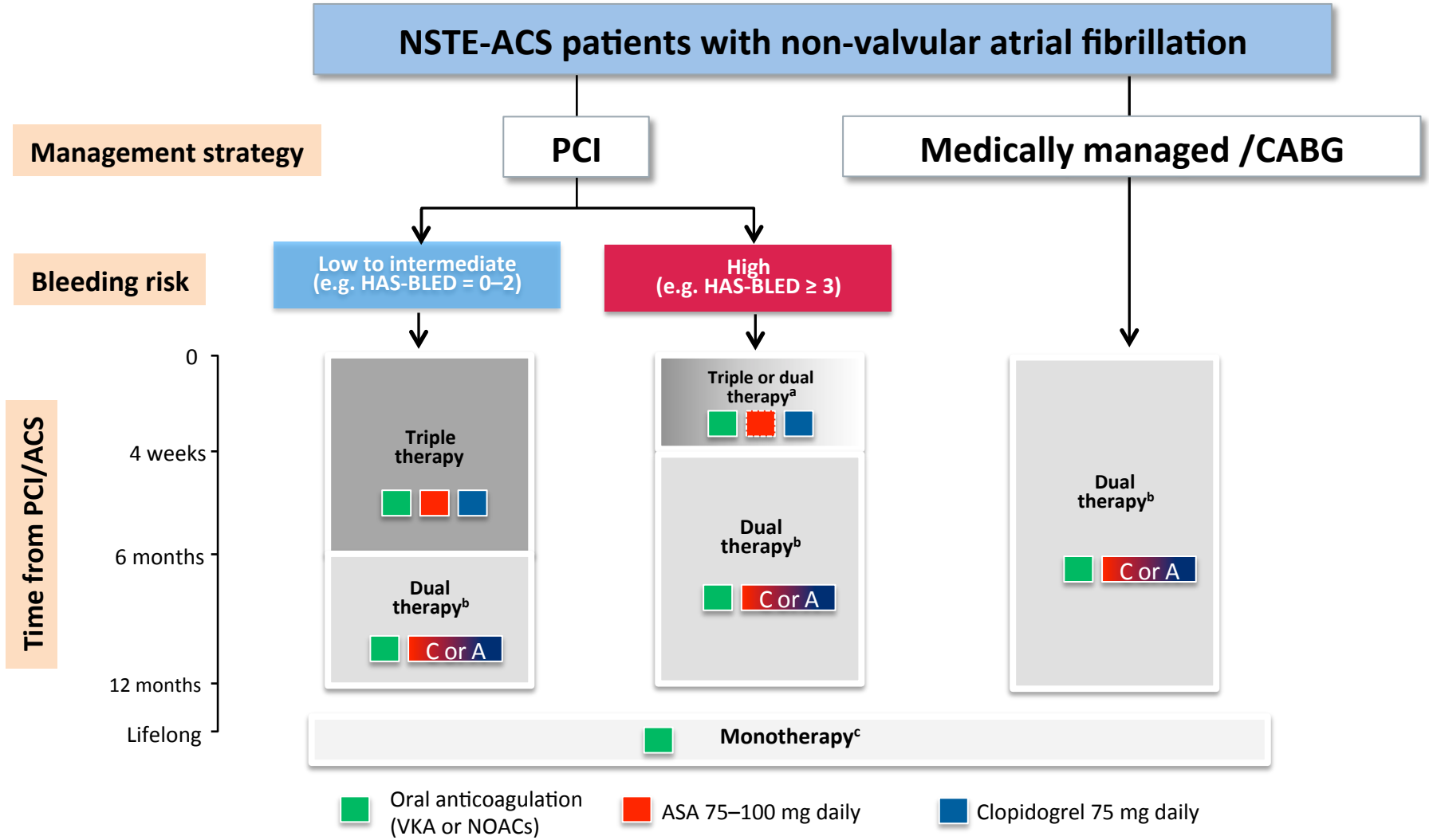


Adapted from Lip et al. Eur Heart J 2014;35:3155–3179.

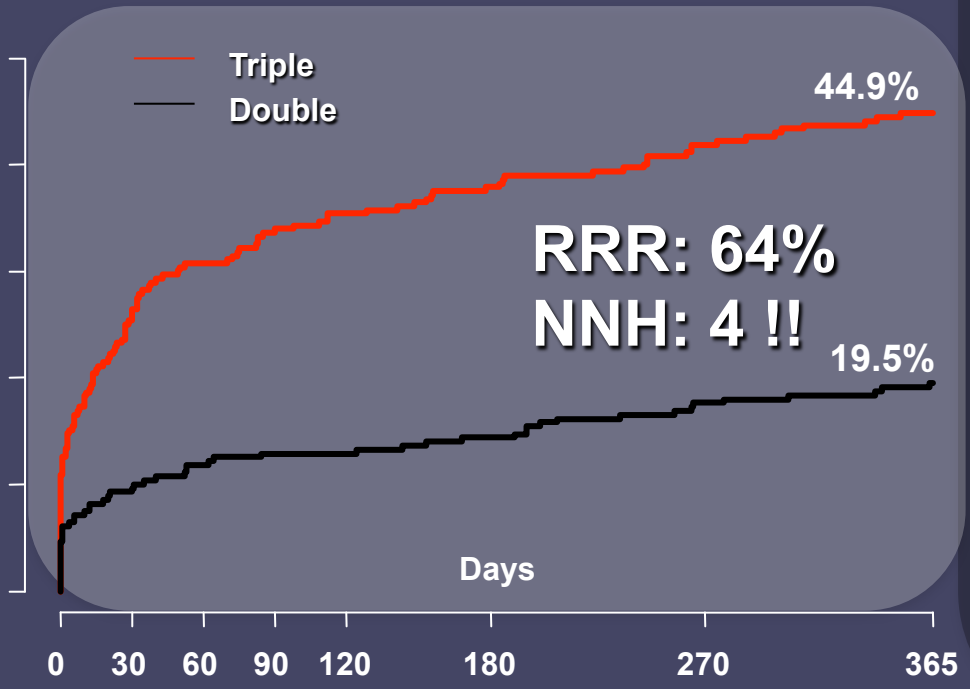
[a]Dual therapy with oral anticoagulation and clopidogrel may be considered in selected patients (low ischaemic risk).

[b]aspirin as an alternative to clopidogrel may be considered in patients on dual therapy (i.e., oral anticoagulation plus single antiplatelet); triple therapy may be considered up to 12 months in patients at very high risk for ischaemic events.

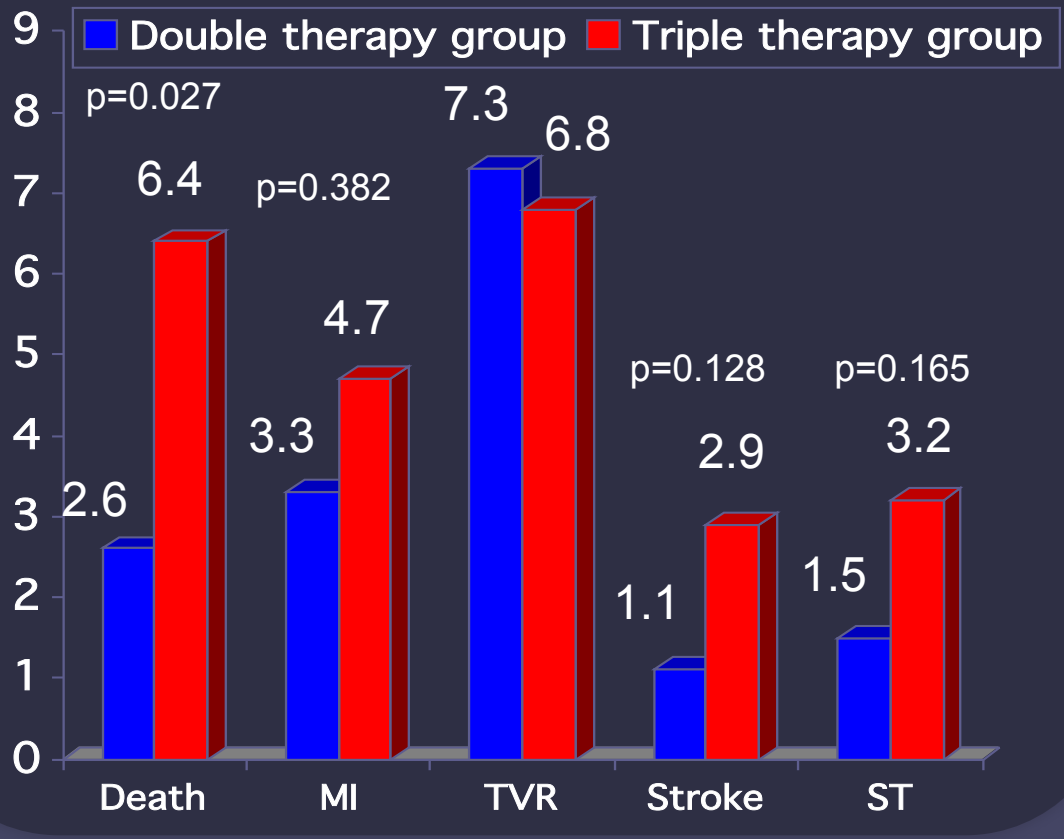
[c]Dual therapy with oral anticoagulation and an antiplatelet agent (aspirin or clopidogrel) beyond one year may be considered in patients at very high risk of coronary events. In patients undergoing coronary stenting, dual antiplatelet therapy may be an alternative to triple or dual therapy if the CHA2DS2-VASc score is 1 (males) or 2 (females).

WOEST Trial

Cumulative incidence of bleeding



Secondary Endpoints



How about patents who do not need OAC ?

GLOBAL LEADERS

Coron… DES …tent implantation

Aspirin
P2Y12i

30 days → 60 days → 90 days → 180 days → ≥360 days → …

All-comers PCI population
(ACS and Stable CAD patients)
(N = 16,000)

Bivalirudin*-supported
BioMatrix family stent implantation
1:1 Randomization, Open-Label Design

Experimental Treatment Strategy		Reference Treatment Strategy	
ASA	P2Y12 i	ASA	P2Y12 i
1 month	24 months	24 months	12 months

Is Aspirin a still contemporary treatment option ?
Is less more ?

Primary Endpoint (Effectiveness): Death or Q wave MI

DSMB has not stopped the study !!

Enrolment

GLOBAL LEADERS

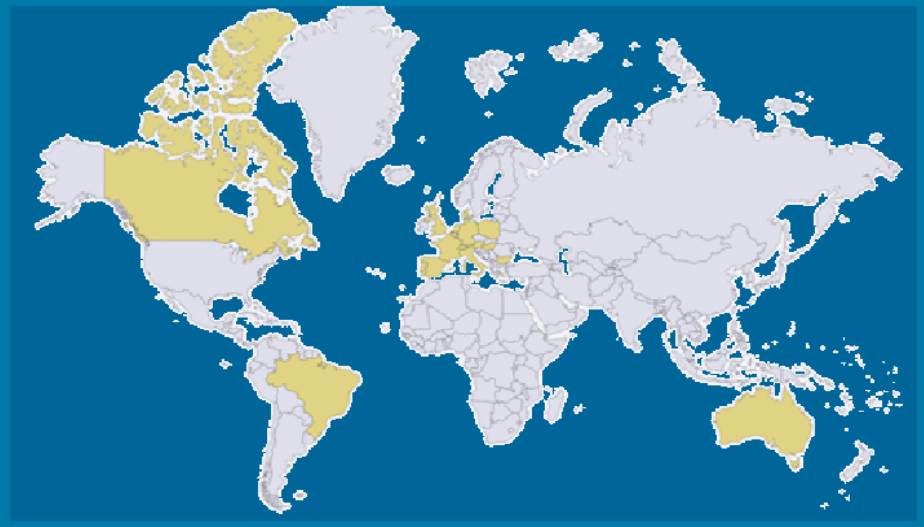
18 Participating Countries

14 European countries:

Germany	17 sites	2278 patients
Belgium	6 sites	2189 patients
United Kingdom	18 sites	1720 patients
Italy	6 sites	1578 patients
Poland	7 sites	1540 patients
The Netherlands	9 sites	1164 patients
Spain	9 sites	952 patients
Bulgaria	8 sites	944 patients
France	13 sites	851 patients
Switzerland	6 sites	706 patients
Austria	5 sites	672 patients
Hungary	8 sites	527 patients
Denmark	2 sites	131 patients
Portugal	4 sites	112 patients

4 non-EU countries:

Brazil	5 sites	248 patients
Canada	2 sites	170 patients
Singapore	2 sites	142 patients
Australia	4 sites	83 patients



TOP 3 RECRUITING COUNTRIES

The ranking is based on amount of patients / amount of active sites

1. BELGIUM	2. ITALY	3. POLAND
365 pts/site	262 pts/site	219 pts/site
6 active sites	6 active sites	7 active sites

"Less is more": Aspirin withdrawal

Post-PCI:

GLOBAL LEADERS (NCT01813435) started on February 2013 (ticagrelor)
TWILIGHT (NCT02270242) started on August 2015 (ticagrelor)
TICO (NCT02494895) started on July 2015 (ticagrelor)

ACS patients:

GEMINI-ACS-1 (NCT02293395) started on April 2015 (rivaroxaban)

Post-ACS:

COMPASS (NCT01776424) started on February 2014 (rivaroxaban)

Post-PCI in AF patients:

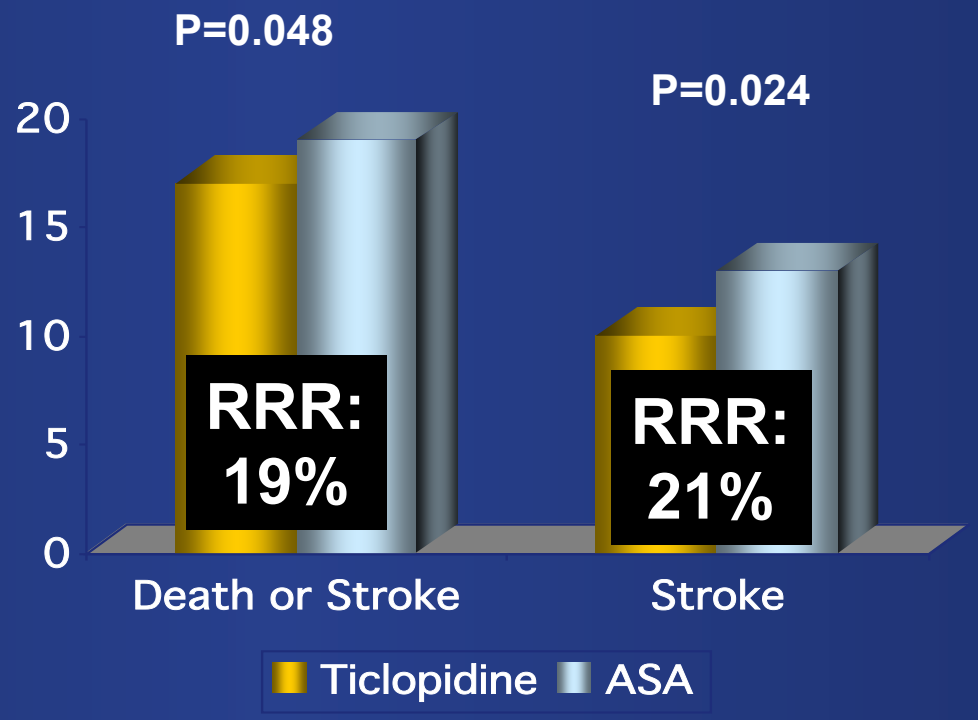
PIONEER AF-PCI (NCT01830543) started on May 2013 (rivaroxaban)
REDUAL-PCI (NCT02164864) started on July 2014 (dabigatran)
AUGUSTUS (NCT02415400) started on June 2015 (apixaban)
ENTRUST AF-PCI going to be registered (edoxaban)

Post-TAVI:

GALILEO (NCT02556203) started on December 2015 (rivaroxaban)
ATLANTIS (NCT02664649) started on February 2016 (apixaban)

Ticlopidine Aspirin Stroke Study (TASS)

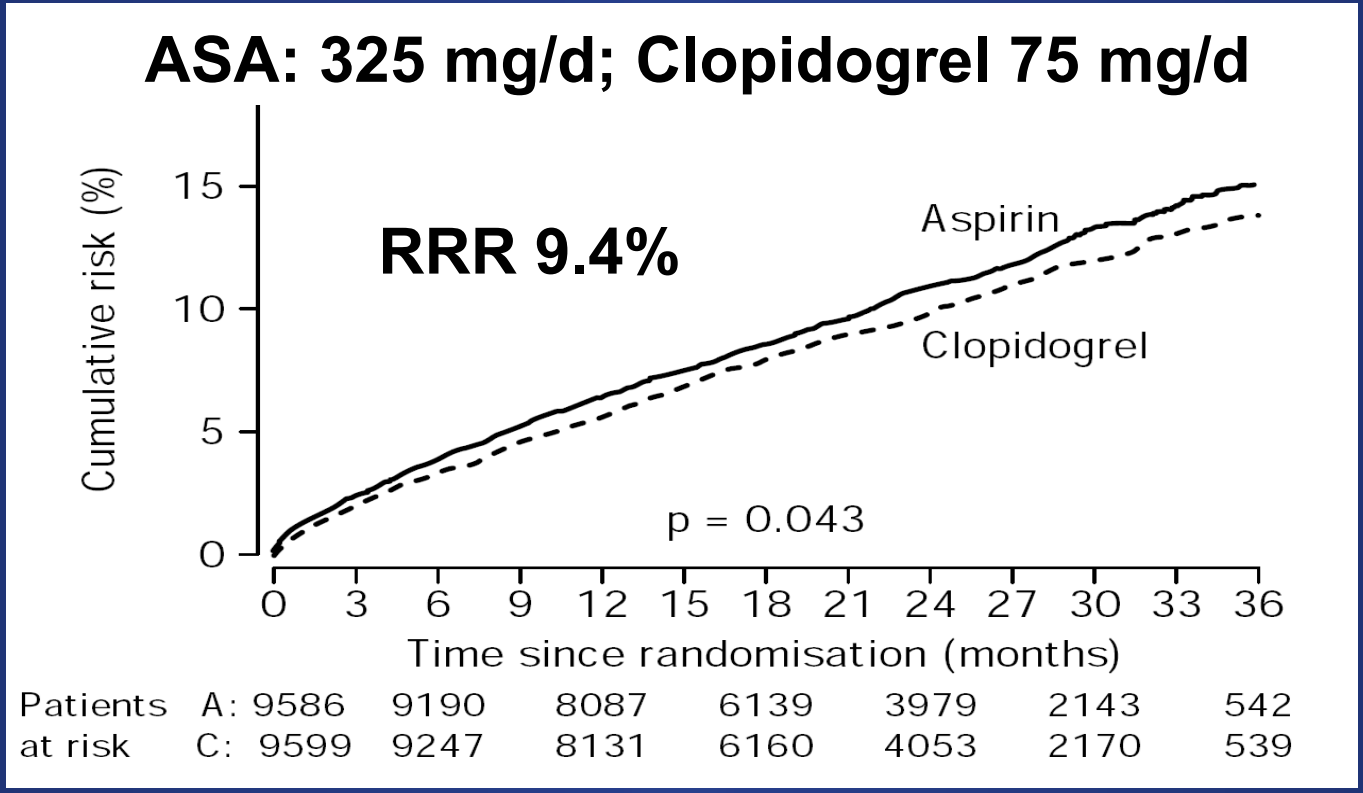
A blinded trial at 56 North American centers that compared the effects of ticlopidine hydrochloride (500 mg daily) with those of aspirin (1300 mg daily) on the risk of stroke or death. The medications were randomly assigned to 3069 patients with recent transient or mild persistent focal cerebral or retinal ischemia. Follow-up lasted for two to six years



N Engl J Med. 1989 Aug 24;321(8):501-7

CAPRIE

19,185 pts; recent stroke, recent MI or PAD

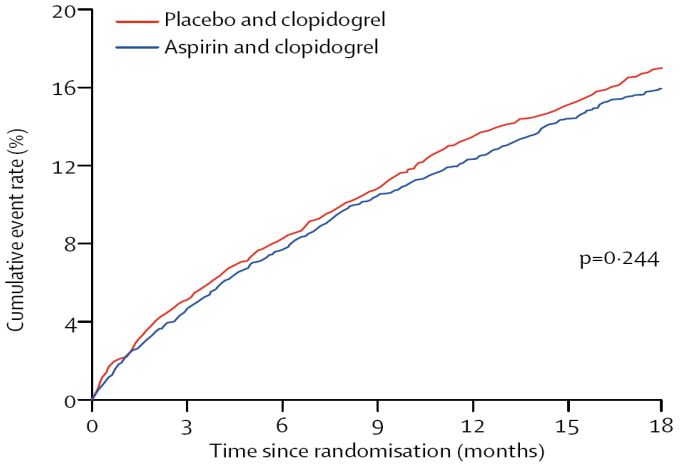


1° EP: Vascular death, MI or stroke

MATCH study

7,599 pts with recent stroke or TIA. All on clopidogrel Randomization to receive ASA or Placebo on top.

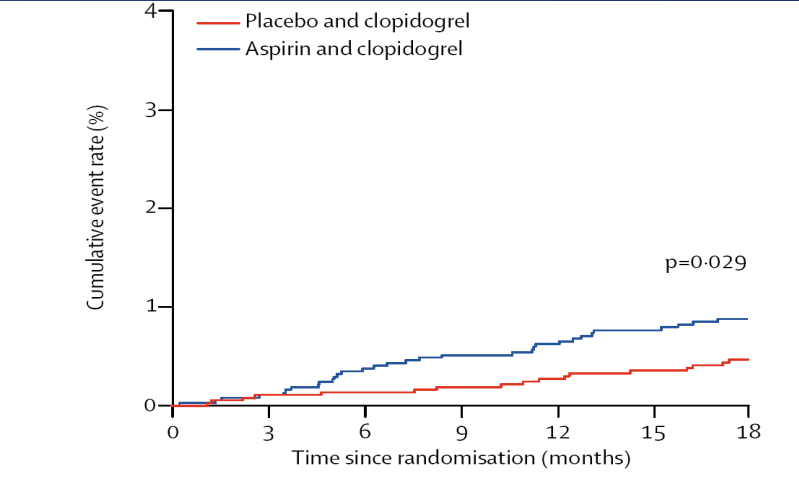
Vascular death, stroke, MI, rehosp for ACS



Patients at risk

Aspirin and clopidogrel	3797	3576	3440	3321	3229	3130	2441
Placebo and clopidogrel	3802	3576	3439	3326	3200	3119	2446

Intracranial bleeding



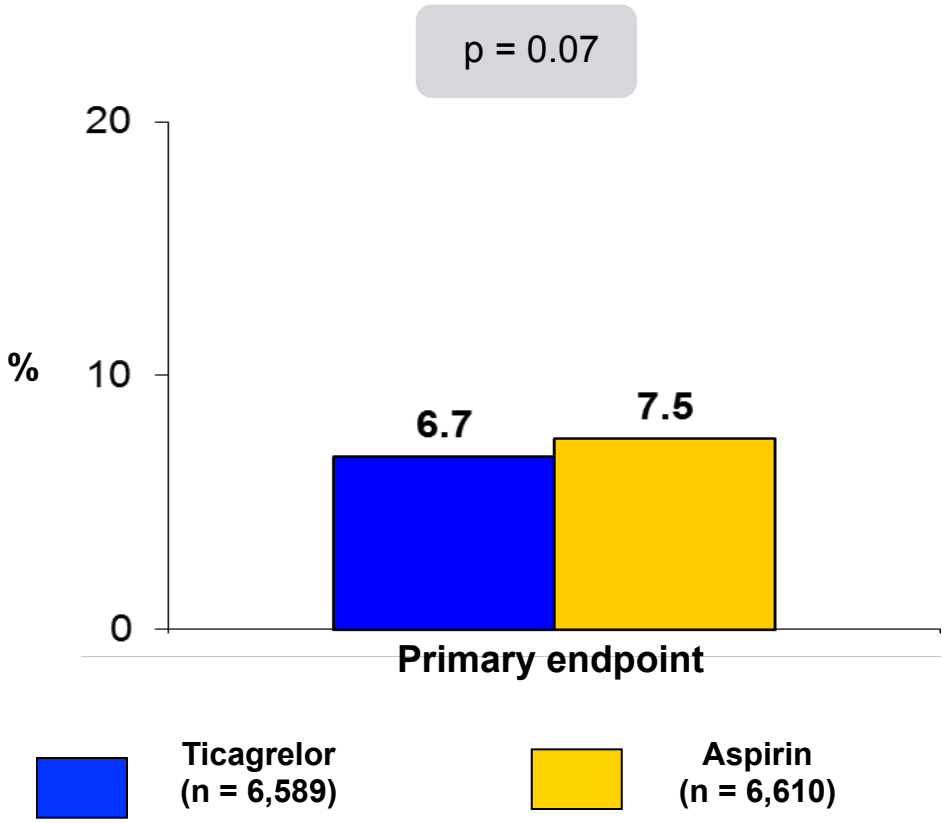
Patients at risk

Aspirin and clopidogrel	3724	3691	3643	3601	3552	3508	2756
Placebo and clopidogrel	3781	3576	3686	3638	3582	3544	2823

Lancet 2004; 364: 331–37

SOCRATES

Trial design: Patients with acute ischemic stroke or TIA were randomized in a 1:1 fashion to receive either ticagrelor 180 mg load + 90 mg BID or aspirin 300 mg load + 100 mg/day within 24 hours of presentation. They were followed for 3 months.



Results

- Primary outcome, death, MI or stroke, for ticagrelor vs. aspirin: 6.7% vs. 7.5%, HR = 0.89, 95% CI 0.78-1.01, p = 0.07
- Death: 1.0% vs. 0.9%, p = 0.36; All strokes: 5.9% vs. 6.8%, p = 0.03; ischemic stroke: 5.8% vs. 6.7%, p = 0.046
- Major bleeding: 0.5% vs. 0.6%, p = 0.45; intracranial hemorrhage: 0.2% vs. 0.3%, p = 0.3

Conclusions

- Ticagrelor monotherapy was not superior to aspirin in reducing cardiovascular events in patients with low-acuity ischemic stroke or high-risk TIA
- Major bleeding was similar
- Unknown if a benefit may be observed on longer duration of follow-up, or in patients with proven ischemic stroke only

Johnston SC, et al. N Engl J Med 2016;May 10:[Epub]

Conclusive Remarks

- It is too early to drop aspirin, the oldest drug still part of our unavoidable anti-thrombotic armamentarium after DES in patients not needing OAC
- This question is being asked
- The Global leaders is the first major study asking this question but a conclusive answer will require consistent evidence coming from multiple RCTs

"having to choose between two evils"