

P: In ED patients suffering from acute stroke or TIA who did not receive TPA

I: Does the use of Aspirin and Plavix (clopidogrel)

C: Compared to Aspirin alone

O: Safely reduce the risk of another CVA

Study	Patient Group	Study Type	Key Outcomes	Key Results	Limitations
Bhatt DL, et. Al. Clopidogrel and aspirin vs aspirin alone for the prevention of atherothrombotic events (CHARISMA). NEJM, 2006; 354: 1706-17.	15,603 pts with >45 yo, multiple atherombotic risk factors, documented CAD, Documented cerebrovascular disease, documented symptomatic PVD 7,802 pts clopidogrel 75 mg plus ASA 75-162 mg qday 7,801 pts placebo plus ASA 75 -162 mg qday	Randomized, controlled, placebo	Primary endpoints: First MI, CVA, Death Secondary: Primary events plus hospitalization for CAD or TIA Safety end point – severe bleeding	Rate of primary events: ASA+clopidogrel: 6.8% ASA: 7.3% RR0.93 CI(0.83-1.05) p=0.22 Secondary Endpoint: ASA+clopidogrel: 16.7% ASA: 17.9% RR0.92 CI(0.86-0.995)p=0.04 Moderate Bleeding: ASA+clopidogrel: 2.1% ASA 1.3% RR1.62 CI(1.27-2.08) p=<0.001	More patients discontinued treatment in ASA+clopidogrel
Diener HC, et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomized, double-blind, placebo-controlled trial. Lancet, 2004; 364: 331-37.	7599 pts with either ischaemic stroke or TIA in the previous 3 months and one or more risk factor – previous ischemic stroke, previous MI, angina pectoris, diabetes, or symptomaticperipheral disease 3759 pts received ASA 75 mg and clopidogrel 75 mg 3802 received placebo and clopidogrel 75 mg	Randomized, controlled, placebo,	Primary Endpoint: First occurrence of an ischemic stroke, myocardial infarction, vascular death, or rehospitalisation for an acute ischaemic event Secondary Endpoint: Combination of primary endpoints, any death, any stroke Life threatening bleeding:	Death: ASA&C 201 vs ASA 201 Ischemic Stroke: ASA&C 309 (8%) vs 333 (9%) p 0.353 Life threatening bleeds: ASA&C – 3%, ASA 1% P<0.0001	Followed patients 18 months

			transfusion of >4 units prbc Severe Bleeding: Transfusion <3 UPRBC		
Sacco RL, et al. Aspirin and extended release dipyridamole versus clopidogrel for recurrent stroke (PROFESS). NEJM, 2008; 359: 1238-50.	20,333 pts with recent ischemic stroke <120 days, >49 yo 10,181 pts ASA (25 mg)+Dipyridamole (200mg) bid 10,151 pts Clopidogrel (75 mg)	Randomized, controlled, double blinded, Noninferiority study	Primary outcome: Recurrent stroke Secondary outcome: Stroke, MI, death from vascular cause Safety: Major bleeding event	Recurrent Stroke: ASA+dipyridamole: 916 Clopidogrel: 898 HR:1.01CI(0.92-1.11) Secondary outcomes: ASA+dipyridamole: 1333 Clopidogrel: 1333 HR:0.99CI(0.92-1.07) Major Hemorrhage: ASA+dipyridamole: 419 Clopidogrel: 365 HR:1.15CI(1.00-1.32) Intracranial hemorrhage: ASA+dipyridamole: 147 Clopidogrel: 103 HR:1.42(1.11-1.83)	Initially compared ASA+dipyridamole vs ASA+clopidogrel (2027 pts followed on this protocol 8months) Protocol also changed during study to include younger patients and less recurrent strokes Significantly more patients taking ASA+dipyridamole stopped treatment
ESPIRIT Study Group. Aspirin plus dipyridamole versus aspirin alone after cerebral ischemia of arterial origin (ESPIRIT): randomized controlled trial. Lancet, 2006; 367: 1665-73.	2739 pts enrolled 1363 pts receive ASA + dipyridamole (30 – 325 mg + 200 mg bid - with preference to extended release formula) 1376 pts ASA alone (30 – 325 mg)	Randomized, placebo controlled, blinded	Primary outcome: Death from vascular cause, nonfatal stroke, nonfatal MI, major bleeding Secondary: Death, major ischemic events, major bleeding	Total Events: A+D-149 A – 192 RR 0.78 (0.64-0.96) p=0.02 Metaanalysis of Pre-ESPS 2, EPSP 2, ESPIRIT: A+D-522 A-636 RR 0.82 (0.74-0.91) p=0.0003	Pt began treatment within 6 months TIA or minor stroke 470 pts received ASA-dipyridamole dosing was not standardized regards to aspirin dipyridamole Statistical calculations centered on HR ratios rather than p values

Clinical bottom line: In acute stroke and following acute stroke, treatment with Aspirin and clopidrogel does **not** provide a significant reduction in risk of death, restroke, or MI. Additionally it does appear to significantly increase the risk of bleeding. There fore treatment should be with Aspirin or Aspirin and Dipyridamole. Just say No to Plavix.