



## Early dual antiplatelet therapy after minor stroke: Does it take two to tango?

### CLINICAL QUESTION

**In acute non-cardioembolic minor ischemic stroke or transient ischemic attack (TIA), does adding a second antiplatelet (like clopidogrel or ticagrelor) to ASA reduce recurrent stroke?**

### BOTTOM LINE

**Compared to ASA alone, clopidogrel plus ASA reduced the risk of stroke from 8.2% to 5.5% but increased the risk of major bleeds from 0.6% to 1.2% at 21 days. Continuing clopidogrel beyond 21 days increased major bleeds without reducing strokes. There is no evidence that ticagrelor is more efficacious in reducing stroke than clopidogrel.**

### EVIDENCE

- Clopidogrel + ASA versus ASA: Time analysis from meta-analysis<sup>1</sup> of 3 randomized controlled trials (RCTs), 10,447 patients:
  - Clopidogrel (300-600mg on day 1, then 75mg/day) plus ASA within 12-24 hours of onset of minor ischemic stroke or high-risk TIA versus ASA alone for 21-90 days, followed by single antiplatelet.
  - At 21 days:

- Ischemic stroke: 5.5% versus 8.2% (ASA), number needed to treat (NNT)=38.
    - Major bleed: 1.2% versus 0.6% (ASA) (number needed to harm [NNH]=167)
  - On days 22-90:<sup>1,2</sup>
    - Ischemic stroke: No difference.
    - Major bleed: 0.6% versus 0.3% (ASA), NNH=334.
- Ticagrelor + ASA versus ASA: One RCT, 11,016 patients:<sup>3</sup>
  - Started ticagrelor (180mg on day 1, then 90mg twice daily) plus ASA within 24 hours of mild-moderate ischemic stroke or TIA versus ASA alone, continued for 30 days.
    - Ischemic stroke: Ticagrelor + ASA 5.0%, ASA 6.3%, NNT=84.
    - Moderate-severe bleed: 0.65% versus 0.2%, NNH~200
      - Intracranial hemorrhage: 0.36% versus 0.11%, NNH~330.
- No significant differences in disability or death between dual and single antiplatelet.<sup>1</sup>

## CONTEXT

- “Minor” stroke defined based on the National Institutes of Health Stroke Scale  $\leq 3-5$ .<sup>1-4</sup>
- Cardioembolic strokes (e.g. related to atrial fibrillation) are treated differently.<sup>5</sup>
- Recurrent stroke risk highest within ~2 weeks of event.<sup>1,2,4</sup>
  - Guidelines recommend clopidogrel + ASA for 21 days in patients with acute non-cardioembolic minor ischemic stroke.<sup>5</sup>
- Clopidogrel or ticagrelor alone have similar efficacy to ASA alone in minor-moderate ischemic non-cardioembolic stroke.<sup>6,7</sup>
- In acute coronary syndromes, ticagrelor + ASA causes more major bleeding and dyspnea (NNH 16) than clopidogrel + ASA.<sup>8</sup>
- Costs per 90 days: ASA \$5, clopidogrel \$40, ticagrelor \$320.9

## REFERENCES

1. Hao, Tampi, O'Donnell M, *et al.* BMJ 2018; 363:k5108.
2. Johnston SC, Elm JJ, Easton JD, *et al.* Circulation 2019; 140:658-64.
3. Johnston SC, Amarenco P, Denison H, *et al.* New Engl J Med 2020; 383:207-17.
4. Pan Y, Jing J, Chen W, *et al.* Neurology 2017; 88:1906-11.
5. Powers WJ, Rabinstein AA, Ackerson T, *et al.* Stroke 2019; 50:e344-e418.
6. Lindblad AJ, Allan GM. Anti-platelets after stroke: Are two better than one? Tools for Practice online publication #109. Published March 17, 2014. Available at: [https://gomainpro.ca/wp-content/uploads/tools-for-practice/1397843680\\_20140317\\_084605.pdf](https://gomainpro.ca/wp-content/uploads/tools-for-practice/1397843680_20140317_084605.pdf) Accessed May 20, 2021.
7. Johnston SC, Amarenco P, Albers GW, *et al.* N Engl J Med 2016; 375:35-43.
8. Wallentin L, Becker RC, Budaj A, *et al.* N Engl J Med 2009; 361:1045-57.
9. Alberta College of Family Physicians Price Comparison of Commonly Prescribed Pharmaceuticals in Alberta 2019. <https://acfp.ca/wp-content/uploads/2019/02/ACFPricingDoc2019.pdf> [accessed 2021 Jan 19]

## AUTHORS

**Ricky D Turgeon**, BSc  
(Pharm) ACPR  
PharmD, **Adrienne J Lindblad**, BSP ACPR  
PharmD, **Jennifer Potter**, MD CCFP

*Authors do not have any conflicts of interest to declare.*