**Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA (THALES trial)**

**Background and Study Objective(s):**

Traditionally ASA alone has been used in the treatment of TIA's and minor ischemic strokes. However, there has been recent evidence suggesting dual antiplatelet therapy (DAPT) reduces the risk of further ischemic events as compared to ASA alone. The CHANCE and POINT trials showed a benefit with DAPT with Clopidogrel. There are some advantages to Ticagrelor compared to Clopidogrel and so the investigators of this study sought out to see if DAPT with Ticagrelor was superior to ASA alone.

**Study Design:**

This was a multicenter, randomized, double blind, placebo controlled, industry funded trial carried out across 414 sites in 28 countries. At total of 11,016 patients with high risk TIA's (defined by ABCD2 scores >5) and minor ischemic strokes (NIHSS <6) were randomized to receive either DAPT with Ticagrelor (loading dose 180mg followed by 90mg BID) and ASA (loading dose plus 81mg daily) or to ASA alone. Exclusion criteria included patients with suspected cardioembolic strokes and patients who were at high risk of bleeding such as history of intracranial hemorrhage or recent surgery or previous GI bleed.

The primary outcome was the incidence of stroke or death at 30 days. Secondary outcomes included the risk of ischemic stroke as well as disability (score >1 on Modified Rankin Score). The primary safety outcome was major bleeding.

**Results:**

Patients in the DAPT treatment arm had a lower risk of death or stroke at 30 days (5.5% vs 6.6%). Recurrent ischemic stroke was 21% less common with DAPT than with ASA alone (5.0% vs 6.3%). Disability outcomes did not differ between the groups. Predictably, severe bleeding was significantly more common in the DAPT group as compared to the ASA alone group (0.5% vs 0.1%). The NNT was 92 and the NNH was 263.

**Validity of Results:**

This study answered a clear, clinically relevant question in the context of clinical equipoise regarding the best way to treat high risk TIA's and minor strokes. The results of this study appear to have good internal validity. It was a well-designed study with a large number of participants.

Limitations include the significant exclusion criteria applied; it is often difficult to determine the cause of the stroke/TIA at first presentation without significantly more investigations which are not practical for most emergency clinicians. There was also a significant number of patients in the treatment arm who withdrew from the trial prematurely due to bleeding concerns. These patients were not analyzed unless they had an outcome event.

Additionally, this was an industry funded trial. The investigators make note about the independence in the writing of the first draft, but ultimately Astrazeneca was represented at the research committee and there were confidentiality agreements in place. This suggests inherent bias towards the treatment arm.

**Generalizability of Results:**

This study was conducted mostly in Europe and Asia in emergency departments with access to CT and MRI facilities. While these healthcare settings and populations are reasonably similar to the settings and patients here in Canada, there may be some ethnic differences along with differences in availability of advanced imaging for these cases, namely MRI.

**The Bottom Line:**

DAPT with ticagrelor after minor ischemic stroke or TIA leads to reductions in death or stroke and recurrent ischemic stroke at 30 days when compared to treatment with ASA alone. However, there is no change in disability and in fact it associated with an increase rate of significant bleeding.

While this is a study that provides a new option for stroke prevention, it highlights the importance of patient centered outcomes. It would have been more impactful for this study to have been powered to detect a difference in disability, as this is what clinicians and patients care about when making the decision to start therapy. This is especially true when the therapy causes a significant increase in serious bleeding. Overall, a NNT of 92 and a NNH of 263 (serious harm) does not seem practice changing.