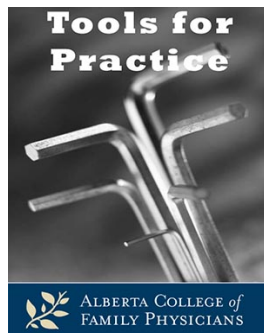


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The new anti-platelet ticagrelor: Is it better than the old "new" clopidogrel?

Clinical Question: How does the newer anti-platelet drug ticagrelor (Brillinta®) compare to clopidogrel for post-acute coronary syndrome (ACS)?

Bottom Line: After ACS, ticagrelor reduces combined cardiovascular death, stroke, and myocardial infarction (MI) about 2% more than clopidogrel. Ticagrelor increases a few adverse events, particularly 6% more dyspnea, and effectiveness remains uncertain in North America.

Evidence:

- PLATO, multinational Randomized Controlled Trial (RCT) of 18,624 patients hospitalized for ACS +/- ST elevation, comparing ticagrelor vs. clopidogrel (both with usual care including ASA) for 12 months maximum,^{1,2} found statistically significant reduction in:
 - Primary endpoint (composite of cardiovascular death, MI, or stroke), Number Needed to Treat (NNT) 53.
 - Other outcomes better:
 - Recurrent MI: NNT 91.
 - Death from vascular causes: NNT 91.
 - Death from any cause: NNT 71.
 - No significant difference in stroke.
 - Adverse reactions:
 - No significant difference in any bleeding except:
 - Bleeding worse when coronary artery bypass patients excluded, Number Needed to Harm (NNH) 143.
 - Worse fatal intracranial hemorrhage, NNH 926.
 - Any dyspnea, NNH 17; Requiring discontinuation, NNH 125.
 - Non-fatal arrhythmias (ventricular pauses) were significantly increased with ticagrelor as well.³
 - Subgroup analysis of 1,800 patients in PLATO from North America showed much less favourable results: mortality was actually lower in clopidogrel group at 12 months.^{2,3}

Context:

- Ticagrelor has several theoretical benefits over clopidogrel: it is a reversible platelet inhibitor, hepatic metabolism not required for activation (less intra-individual variability in response), and faster onset/offset of action.^{3,4}
- Benefits of ticagrelor seem maintained in higher risk groups like those with renal insufficiency⁵ and diabetes.⁶
 - Ticagrelor proposed as an alternative in clopidogrel non-responders.⁷
- Unanswered concerns:
 - No clear explanation why ticagrelor worse in North America.⁸
 - Dyspnea unexplained³ but is not associated with structural cardiac damage or pulmonary function test abnormalities.^{9,10}
- Ticagrelor is significantly more expensive than clopidogrel (\$310/90 days vs. \$100/90 days)¹¹ and requires twice-daily dosing.
- Given the cost, increased harms, and uncertainty around effectiveness in North America, clinicians should:
 - Consider clopidogrel a reasonable alternative in intolerant patients started on ticagrelor in hospital.

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Disclosure:

Authors have no conflicts to disclose.

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