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Evidence Updated: None, slight wording changes; prices updated in Context
Bottom Line: Wording changes
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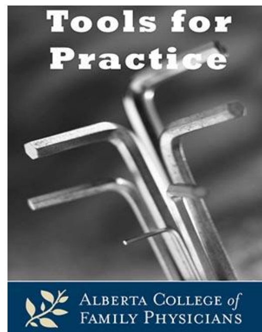

The New Antiplatelet Ticagrelor: Is it better than the old "new" clopidogrel?

Clinical Question: How does the newer antiplatelet 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, is more expensive, and requires BID administration.

Evidence:
PLATO, multinational Randomized Controlled Trial (RCT):

- 18,624 patients hospitalized for ACS, comparing ticagrelor versus clopidogrel (both with usual care including ASA) for up to 12 months,[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 any cause (NNT=71) or vascular causes (NNT=91).
    - 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 of unclear significance (ventricular pauses) were significantly increased with ticagrelor as well.[3]
  - Subgroup analysis of 1,800 patients in PLATO from North America showed unclear effect, however, these analyses were underpowered and confounded by use of higher doses of ASA than recommended (325 mg daily).[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 insufficiency[5] 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 unexplained,[3] 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 versus $60/90 days)[11] and requires twice-daily dosing.
- Clopidogrel remains a reasonable alternative, particularly if patients:
  - Are at high risk of bleeding.
  - Cannot tolerate ticagrelor because of dyspnea.
  - Cannot adhere to ticagrelor's BID dosing.
  - Cannot afford ticagrelor.

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Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicianswho are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at http://bit.ly/signupfortfp. Archived articles are available on the ACFP website.

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