Acute coronary syndrome without revascularisation: prasugrel versus clopidogrel

A large randomised controlled trial in people with unstable angina or non ST-segment elevation myocardial infarction but who had not had revascularisation, found no difference in important patient-oriented outcomes between prasugrel and clopidogrel. Similar rates of severe and intracranial bleeding were observed between the two groups. Current NICE guidance only covers the use of prasugrel in those with ACS who have undergone revascularisation.

Overview and current advice

The term 'acute coronary syndromes' (ACS) encompasses a range of conditions from unstable angina to ST-segment-elevation myocardial infarction (STEMI), arising from thrombus formation on an atheromatous plaque.¹

NICE guidance on unstable angina and non ST-segment elevation myocardial infarction (NSTEMI) and NICE guidance on MI – secondary prevention advise that a combination of low-dose aspirin and clopidogrel 75mg daily is recommended for the medical management of both non-ST segment-elevation ACS¹ and ST segment elevation MI². Combination treatment should be continued for 12 months after the most recent acute episode of non-ST-segment-elevation ACS¹ and, in those treated within the first 24 hours, at least one month after the most recent acute episode of STEMI². Thereafter, standard treatment including low-dose aspirin should be given, unless there are other indications to continue dual antiplatelet therapy¹,². Current NICE guidance only covers the use of prasugrel in those with ACS who have undergone revascularisation, where its use in combination with aspirin is recommended as an option under specific circumstances.³

Healthcare professionals should be aware of the potential risk of rare but serious hypersensitivity reactions with prasugrel and should monitor for signs in all patients, including those with a previous known history of hypersensitivity reactions to thienopyridines, for example, clopidogrel⁴. When prescribing prasugrel, prescribers should inform patients of the potential risk of hypersensitivity reactions, including angioedema⁵. Suspected adverse reactions to prasugrel should be reported via the Yellow Card Scheme. More information is available in May 2011 Drug Safety Update from the MHRA and in a letter for healthcare professionals.
New evidence

This double-blind, randomised trial (TRILOGY ACS; Roe M.T. et al, 2012) aimed to evaluate whether prasugrel (10 mg daily, reduced to 5 mg for those weighing under 60 kg) is superior to clopidogrel (75 mg daily) for long-term therapy in 7243 people with ACS (unstable angina or non-STEMI). Patients included in the study had at least one of four risk criteria: an age of at least 60 years, the presence of diabetes mellitus, previous MI, or previous revascularisation. All participants were also receiving aspirin. Additionally, a secondary analysis was carried out which explored a lower prasugrel dose (5 mg daily) versus clopidogrel (75 mg daily) in 2083 people 75 years and older.

In the main analysis of patients under the age of 75 years, at 30 months there was no statistically significant difference between the prasugrel group and the clopidogrel group in the rate of the primary end point (death from cardiovascular causes, MI, or stroke): prasugrel 13.9%, clopidogrel 16.0% (95% confidence intervals [CIs] 0.79 to 1.05, p = 0.21). Similar results were observed in the overall population of 9326 people of all ages who underwent randomisation. A prespecified analysis of multiple recurrent ischemic events (all components of the primary end point) suggested a lower risk for prasugrel among patients under the age of 75 years, although this just reached statistical significance (hazard ratio, 0.85; 95% CI, 0.72 to 1.00; p = 0.04). Rates of severe and intracranial bleeding were similar in the two groups in all age groups. There was no significant difference between groups in the frequency of non-haemorrhagic serious adverse events, except for a higher frequency of heart failure in the clopidogrel group.

Since NICE guidance on prasugrel for the treatment of acute coronary syndrome with percutaneous coronary intervention was published the price (and consequently the cost-effectiveness) of clopidogrel has changed because of the availability of generic dosage forms. At the time of writing, the current price of clopidogrel was £25.35 for 13x28 days of treatment while the current price of prasugrel was £618.28 for 13x28 days of treatment. Therefore, the Institute’s Guidance Executive has decided that a review of the guidance (TA182) should be planned into the appraisal work programme.

See the NHS Evidence topic page on acute coronary syndromes for a general overview of the condition.

Commentary

Commentary provided by: Dr Raj Khattar DM FRCP FACC FESC, Consultant Cardiologist and Honorary Clinical Senior Lecturer, Royal Brompton Hospital and Imperial College, London:

Patients who present with an acute coronary syndrome should, as far as possible, undergo invasive coronary angiography with a view to revascularisation. However, some of these patients are managed medically because of advanced age or prohibitive co-morbidities such as renal dysfunction and chronic lung disease. These patients are at an inherently high risk of subsequent adverse cardiac events. Dual anti-platelet therapy with aspirin and clopidogrel given for a period of 12 months is standard treatment for ACS patients not undergoing revascularisation.

The TRILOGY ACS study in ACS patients not undergoing revascularisation found no advantage for prasugrel over clopidogrel in terms of efficacy or safety. Now that generic clopidogrel is available at much lower cost, this is likely to have an impact on the cost-effectiveness of prasugrel in this group of patients. One point of interest was that a sub-study comparing a lower dose of prasugrel 5 mg a day in patients aged over 75 years or weighing under 60 kg also showed similar efficacy to clopidogrel 75 mg a day. However, it should not be extrapolated that prasugrel 5 mg a day would be equally effective in such patients undergoing revascularisation for STEMI as these patients tend to have a higher thrombus burden and efficacy of the lower dose of prasugrel in these patients has not been studied. Consequently, in my opinion, the use of prasugrel should remain limited to previously published NICE guidance.
References

6. NHSBSA. Drug Tariff, accessed online 12th December 2012

About this Medicines Evidence Commentary

Medicines Evidence Commentaries form part of NICE’s Medicines Awareness Service and help contextualise important new evidence, highlighting areas that could signal a change in clinical practice. They do not constitute formal NICE guidance. The opinions of contributors do not necessarily reflect the views of NICE.

Visit Evidence Search

Copyright © 2013 National Institute for Health and Care Excellence. All Rights Reserved.