

Drug Watch

Prasugrel, a new antiplatelet drug

In patients with ST-segment-elevation MI (STEMI) undergoing percutaneous coronary intervention (PCI), treatment with a new antiplatelet agent prasugrel significantly reduced ischemic events compared with clopidogrel, without a significant increase in bleeding risks [1]. In February 2009 the EMEA granted marketing approval of prasugrel for the prevention of atherothrombotic events in patients with acute coronary syndrome undergoing PCI; the FDA is still deliberating.

The results, from a pre-specified analysis of the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel (TRITON-TIMI 38), showed that treatment with prasugrel resulted in significant reductions in 30-day rates of cardiovascular death, nonfatal MI, or nonfatal stroke, a benefit that persisted to 15 months. In addition, there were reductions in secondary endpoints, including a significant reduction in stent thrombosis rates, with prasugrel.

However, all-cause and cardiovascular mortality rates were similar between the two treatments at 15 months. Safety data showed that prasugrel was associated with more instances of bleeding than clopidogrel, including life threatening and fatal episodes.

An accompanying editorial notes several limitations of the study: the low dose of the comparator drug and the fact that late enrollees did not receive the full benefit of clopidogrel.

So are the advantages really clear?

1. Lancet. doi:10.1016/S0140-6736(09)60441-4.

Azacitidine, a new drug for blood cancers

A recent trial [1] finds that treatment with azacitidine (Vidaza) increases overall survival in patients with higher-risk myelodysplastic syndromes. In patients who are not eligible for stem cell transplantation, azacitidine nearly doubled two-year survival rates. Although the side effects are very common and unpleasant, patients receiving azacitidine experienced 25% fewer hospital admissions per year and required one-third fewer IV antibiotics to treat infections. The drug has now been approved by the EMEA as well as the FDA.

Azacitidine is an anti-neoplastic pyrimidine nucleoside analogue used to treat several subtypes of myelodysplastic syndrome and acute myeloid leukaemia. The drug exerts a cytotoxic effect on rapidly dividing cells, including cancerous cells, and may help restore normal function to genes controlling proper cellular differentiation and proliferation.

1. Lancet Oncol. doi:10.1016/S1470-2045(09)70003-8.

Best blood glucose range in ICU patients remains unclear

Two studies of intensive versus conventional glucose control in critically ill patients suggest that rigorous glucose control in patients in ICUs is associated with an increased risk of death.

Tightly regulated blood sugar has been recommended for critically ill patients.

However, an Australian/New Zealand trial found that 829 of 3,010 patients in the intensive-control group had died, compared with 751 of 3,012 patients in the conventional-control group ($p = 0.02$), which was still significant after adjustment for the predefined baseline risk factors. The study authors say that it is unclear as to whether the deaths were due to reduced blood glucose level, increased administration of insulin, occurrence of hypoglycaemia, methodological factors specific to the trial, or other factors.

Following a meta-analysis of 26 trials [2] the authors suggest "policy makers reconsider recommendations promoting the use of intensive insulin therapy in all critically ill patients."

1. N Engl J Med. 2009;360:1283.

2. Can Med Assoc J. 2009;8:821.

Drug resistance and hepatitis B

The Lancet Infectious Diseases has reviewed the prevention and management of drug resistance during the management of hepatitis B infection.

Emergence of drug resistance in antiviral therapy for chronic hepatitis B negates treatment benefits. There is a lower chance of resistance emerging if drugs rapidly suppress viral load and this also makes mutations less likely. Measurement of viral load at 24 weeks' treatment to aid decision-making is mandatory for patients receiving drugs that are associated with a higher resistance rate. Combination treatment with drugs that belong to different groups is associated with a lower chance of resistance. To ensure better control of viral replication in patients with drug resistance, the addition of another drug without an overlapping resistance profile should be given as early as possible, preferably at the time when genotypic resistance emerges. With such strategies, most patients can be maintained in clinical remission.

Lancet Infect Dis. doi:10.1016/S1473-3099(09)70056-8.