

## Two new treatments for metastatic melanoma

Following 30 years of stasis in the treatment of metastatic melanoma, two trials reported at the American Society of Clinical Oncology meeting in Chicago offer new treatment options for these patients.

More than 11 700 people in the UK are diagnosed with metastatic melanoma each year, and over 2000 people die from it each year. Over the last 30 years, the rate of metastatic melanoma in Britain has risen faster than any of the top 10 cancers in males and females. Currently, there are no approved treatments in Europe which have demonstrated an overall survival benefit.

In a phase III randomized controlled trial (Robert et al, 2011) patients with metastatic melanoma who were treated with ipilimumab in combination with dacarbazine (the only approved standard chemotherapy) survived for significantly longer than those treated with

dacarbazine alone (overall survival rate was 47.3% vs 36.3% at 1 year). Metastatic melanoma is an aggressive disease with a median overall survival of 6–9 months and a 1-year survival rate of 25%.

Dr James Larkin, Consultant Medical Oncologist at the Royal Marsden Hospital, one of the leading trial centres for ipilimumab in the UK, commented: 'The new data are significant as ipilimumab is the first treatment which has demonstrated in randomized clinical trials that it can potentially control advanced melanoma for a prolonged period. Currently, the prognosis for these patients is very poor, so this treatment has the potential to make a huge difference to patients' lives.'

Another trial showed that a new pill that precision targets the activity of a faulty gene present in half of terminally ill metastatic melanoma patients significantly extends overall

survival compared to standard chemotherapy (Chapman et al, 2011). Data from the BRIM3 study show that at 6 months 84% of patients with the mutated BRAF gene who received vemurafenib were alive compared to 64% who received dacarbazine.

Treatment with vemurafenib reduced the risk of death by 63% during the follow-up period compared to treatment with dacarbazine (hazard ratio=0.37,  $P<0.0001$ ). Vemurafenib also significantly improved the progression-free survival by 74% compared to chemotherapy (hazard ratio=0.26,  $P<0.0001$ ).

Chapman PB, Hauschild A, Robert C et al; BRIM-3 Study Group (2011) Improved survival with vemurafenib in melanoma with BRAF V600E mutation. *N Engl J Med* 364(26): 2507–16

Robert C, Thomas L, Bondarenko I et al (2011) Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. *N Engl J Med* 364(26): 2517–26

### Decline in heart attacks may be reversed by rising body mass index

A paper published in the *European Heart Journal* reports that, among 9453 people taking part in the long-running Whitehall II study, there was a substantially reduced risk (74%) of a first heart attack among both men and women between 1985 and 2004. However, there was a steady annual rise in body mass index for both men and women, associated with an increase in the risk of heart attack of 11%.

### Low-dose alteplase for occluded central venous access devices

Actilyse Cathflo 2 mg is a low-dose vial of alteplase which can be used to restore the patency of central venous access devices, including those used in haemodialysis.

### People with diabetes will benefit from new surgical guidance

Published by NHS Diabetes, the 'Management of adults with diabetes undergoing surgery and elective procedures: improving standards' aims to raise standards of care for people with diabetes undergoing operative or investigative procedures requiring a period without food.

## Combinations of common drugs increase risk of cognitive impairment and death in older people

Combinations of some common prescription and over the counter drugs can increase the risk of death in older people, according to the results of a 2-year longitudinal study of over 13 000 people aged over 65 years (Fox et al, 2011).

At baseline, 47% used a medication with possible anticholinergic properties, and 4% used a drug with definite anticholinergic properties. After adjusting for age, sex, educational level, social class, number of non-anticholinergic medications, number of comorbid health conditions, and cognitive performance at baseline, use of medication

with definite anticholinergic effects was associated with a 0.33 point greater decline in mini-mental state examination score (95% confidence interval=0.03–0.64,  $P=0.03$ ) than not taking anticholinergics, whereas the use of possible anticholinergics at baseline was not associated with further decline (0.02, 95% confidence interval=-0.14–0.11,  $P=0.79$ ).

Two-year mortality was greater for those taking definite (odds ratio=1.68; 95% confidence interval= 1.30–2.16;  $P<0.001$ ) and possible (odds ratio=1.56; 95% confidence interval= 1.36–1.79;  $P<0.001$ ) anticholinergics.

It also found that people who were already experiencing cognitive impairment declined more quickly when taking several of these drugs, which include antidepressants, tranquilizers, bladder medication and glaucoma eye drops. This was believed to be caused by side effects of the drugs depressing the activity of acetylcholine.

Fox C, Richardson K, Maidment ID et al (2011) Anticholinergic Medication Use and Cognitive Impairment in the Older Population: The Medical Research Council Cognitive Function and Ageing Study. *J Am Geriatr Soc* doi: 10.1111/j.1532-5415.2011.03491.x. (Epub ahead of print 24 June)