Trial watch

FOLIC ACID AND COLORECTAL CANCER RISK

A recent randomized, placebo-controlled study indicates that folic acid supplementation does not lower the risk of colorectal adenomas, and instead might actually increase risk.

Men and women in the US with a history of colorectal adenomas, but no history of invasive carcinoma, were randomized to receive either 1 mg a day of folic acid (n = 516) or placebo (n = 505). Follow-up included one colonoscopy after 3 years of treatment and a second 3–5 years later. The incidence of colorectal adenomas was not reduced by folic acid during the first or second follow-up periods, or when data from both periods were examined together. Similarly, folic acid did not reduce the incidence of advanced adenomas or multiple adenomas, and in fact there was a trend for incidence to be higher in patients who took folic acid. Furthermore, folic acid did not appear to be beneficial even in subgroups of patients who might be more likely to benefit (for example, those who drank alcohol or who had low baseline folate levels).

Around the time this study was initiated, the US began fortifying its food supply with folic acid, which might have affected the outcome of this study. The possible link between folic acid and an increased risk of adenomas and the effects of folic acid-fortification of food should be studied further.

ORIGINAL RESEARCH PAPER Cole, B. F. *et al.* Folic acid for the prevention of colorectal adenomas. *JAMA* **297**, 2351–2359 (2007)

IMMUNOTHERAPY FOR LUNG CANCER

A phase III trial of the melanoma-associated antigen 3 (MAGE-A3) antigen-specific cancer immunotherapeutic (ASCI) as adjuvant therapy in non-small-cell lung cancer (NSCLC) was announced by GlaxoSmithKline following the presentation of positive phase II data at the recent American Society of Clinical Oncology (ASCO) meeting. With a planned enrolment of 2,270 patients, this is the largest phase III trial ever initiated in lung cancer.

MAGE-A3 is a tumour-specific antigen expressed by 35–50% of early NSCLC tumours. MAGE-A3 ASCI includes purified recombinant MAGE-A3 delivered with an immune-stimulating proprietary adjuvant system.

The phase II placebo-controlled study randomized 182 patients with completely resected stage IB or II NSCLC whose tumours expressed MAGE-A3. After a median follow-up of 28 months, relapse was 30.6% in the MAGE-A3 ASCI group and 43.3% in the placebo group, which corresponded with a 27% reduction in the relative risk of relapse following surgery. This difference was not statistically significant ($P = 0.107$), but the study was not powered to show statistical significance, and the trend was encouraging enough to initiate the phase III trial. Furthermore, MAGE-A3 is also expressed by other cancers, so it is possible that this therapy might prove useful for other tumour types.

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