Combined HPV and Pap testing is a potentially beneficial screening approach

Cervical screening by the Papanicolaou (Pap) test substantially reduces the incidence of invasive cervical cancer, but this cancer continues to be a major cause of death in women. Combined Pap and human papillomavirus (HPV) testing might be better than the Pap test alone to detect grade 3 cervical intraepithelial neoplasia, a known precursor of invasive cervical cancer. Naucler *et al*. carried out a population-based, randomized, controlled trial in women aged 32–38 years to test this hypothesis.

A total of 12,527 women underwent HPV plus Pap testing or a Pap test only. Women with a positive HPV and normal Pap results were offered another HPV test at least 1 year later. If persistent infection was present women were offered colposcopy with cervical biopsy.

During the 4-year follow-up, grade 2 or 3 cervical intraepithelial neoplasia or cancer was 51% more common among women who underwent both tests than among those who were tested by Pap alone. At subsequent screenings, risk of grade 2 or 3 lesion in the group initially given both tests was reduced by more than 40%, compared with women who had only Pap smears.

The authors conclude that use of a combined HPV and Pap test to screen women in their mid-30s for cervical cancer might enable intervals between testing to be extended. Longer intervals could lead to lower costs, and possibly reduce mortality among women who attend for screening less frequently than currently recommended.

Original article Naucler P *et al.* (2007) Human papillomavirus and Papanicolaou tests to screen for cervical cancer. *N Eng J Med* **357:** 1589–1597

Complete estrogen blockade in advanced postmenopausal receptor-positive breast cancer

Inhibition of estrogen synthesis with third-generation aromatase inhibitors (AIs) is standard first-line therapy in postmenopausal women with hormone-receptor-positive locally advanced or metastatic breast cancer. Combining an AI with a selective estrogen receptor modulator (SERM) could achieve complete estrogen blockade and be more effective than AI monotherapy. Adding tamoxifen to the AI anastrozole was unsuccessful; Goss *et al.* report success from combining tamoxifen's less estrogenic analog toremifene, with the steroidal AI atamestane.

Postmenopausal women ($n = 865$) with advanced receptor-positive breast cancer, who had completed adjuvant hormonal therapy >12 months previously, were recruited across the US, Canada, Russia and the Ukraine; 434 patients were randomly assigned to atamestane 500 mg/day plus toremifene 60 mg/day, and 431 to the nonsteroidal AI letrozole 2.5 mg/day. Median time to progression was 11.2 months in both arms. Overall survival was slightly higher with the combination (3.01 vs 2.79 years), but objective response was lower (30% vs 36%). Disease progression and clinical benefit (objective response plus stable disease) were similar in the two arms, and the regimens were fairly equally tolerated.

This, say the authors, is the first evidence of an endocrine therapy comparable to letrozole in the treatment of advanced endocrine-responsive breast cancer; an antiestrogen can, therefore, be added to an AI without interfering with its action. Trials of more-potent SERMs and selective estrogen receptor downregulators are underway.

Original article Goss P *et al.* (2007) Phase III, double-blind, controlled trial of atamestane plus toremifene compared with letrozole in postmenopausal women with advanced receptor-positive breast cancer. *J Clin Oncol* **25:** 4961–4966

Patients who survive 10 years after resection of colorectal liver metastases are cured

Over 60% of recurrences after resection of a primary colorectal tumor involve the liver, which is the sole site of metastatic disease in 20–35% of patients. In selected patients, 5-year survival rates of 27–39% have been reported in those with resection of colorectal liver metastases (CLM). Median survival of up to 21 months can be achieved among patients with unresectable metastases treated with chemotherapy. Although many accept resection as the only treatment associated with long-term survival, the rate of true cure is unknown.

With the intention of defining cure after resection of CLM, Tomlinson *et al*. performed

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