Fenretinide can halve the risk of second breast cancer in premenopausal women

A 15-year follow-up study by Veronesi *et al*. has demonstrated that the synthetic retinoid fenretinide can reduce the risk of second breast cancer by 50% in premenopausal women aged 40 years or younger with early-stage breast cancer.

The researchers analyzed data from a subgroup of 1,739 women enrolled in a phase III trial of fenretinide efficacy and who continued long-term follow-up at the Istituto Nazionale Tumori in Milan, Italy. Women with a diagnosis of stage I primary breast cancer who had received first-line therapy were randomized to undergo either observation or treatment with fenretinide 200 mg daily for 5 years. Incidence of both contralateral and ipsilateral second breast cancers was recorded. After a median follow-up of 14.6 years, the rate of second breast cancers in the fenretinide group was 17% lower than in the observation group. When the data were stratified by menopausal status, however, premenopausal women receiving fenretinide had a significantly lower risk of developing second breast cancer than postmenopausal women (hazard ratio 0.62; 95% CI 0.46–0.83). Hazard curves indicated that fenretinide reduces risk by 51% and 48% in women aged 35 years or younger and 40 years or younger, respectively. This protective effect lasted for up to 15 years; that is, up to 10 years after completion of fenretinide therapy.

The authors conclude that these data provide the rationale for a trial of fenretinide chemoprevention in healthy premenopausal women at high risk of breast cancer, such as those with *BRCA1* or *BRCA2* mutations.

Original article Veronesi U *et al.* (2006) Fifteen-year results of a randomized phase III trial of fenretinide to prevent second breast cancer. *Ann Oncol* **17:** 1065–1071

Predicting survival in patients with Kaposi's sarcoma

Researchers in the UK have developed a prognostic index to predict survival in individuals with AIDS-associated Kaposi's sarcoma. Survival varies considerably between patients with this condition, and accurate prognosis is necessary to deliver appropriate treatment. To develop the model, the investigators reviewed the records of 5,873 patients, 326 of whom had Kaposi's sarcoma; they then validated the model in an independent group of 446 patients with the disease. The prognostic index uses a scale of 0–15, with 10 as the base point to avoid negative integers.

Good prognosis was associated with having Kaposi's sarcoma as the first AIDS-defining illness (–3 points on the prognostic index) and with increasing $CD4^+$ cell count (–1 point for every 100 cells per mm^3); poor prognosis was associated with age ≥50 years (+2 points) and with having an additional AIDS-associated illness (+3 points). For individuals with scores of 0, 5, 10 and 15, 1-year probability of survival was 0.993, 0.967, 0.834 and 0.378, respectively; 5-year probability of survival was 0.984, 0.918, 0.631 and 0.084, respectively. Surprisingly, gastric or pulmonary Kaposi's sarcoma, although associated with greatly reduced survival in univariate analysis, was not found to be an independent predictor of survival by multivariate analysis.

The authors recommend that patients with a poor prognosis (score >12) should receive systemic chemotherapy in addition to highly active antiretroviral therapy, whereas low-risk patients (score <5), even those with T1 disease, should receive antiretroviral treatment alone. Further research will help to determine the best approach for patients with an intermediate score.

Original article Stebbing J *et al.* (2006) A prognostic index for AIDS-associated Kaposi's sarcoma in the era of highly active antiretroviral therapy. *Lancet* **367:** 1495–1502

Hypofractionated radiotherapy reduces local breast cancer recurrence

A paper recently published in *The Lancet Oncology* suggests that breast cancer has a similar sensitivity to radiation fraction size as the surrounding healthy tissues. The implication is that radiotherapy for breast cancer could be delivered in fewer, larger fractions without compromising treatment efficacy.

In 1986, a randomized trial was initiated to assess the late effects of radiotherapy fraction size on healthy tissues and the incidence of tumor recurrence in 1,410 women with invasive breast cancer who had undergone local tumor excision. Patients were randomized to receive