or older. The retrospective review included 6,487 patients who received differing chemotherapy doses, schedules and durations.

The analysis found that there was no association between age and survival, although there was an increased risk of breast cancer recurrence in older patients due to a higher percentage with involvement of 10 lymph nodes or over. Analysis also showed that the degree of chemotherapy was significantly related to disease-free survival in all age groups. Treatment-related toxicity was greater in older patients compared with younger patients and increased linearly with increasing age. There was an age bias in the trials towards younger patients—despite the fact that around 50% of new breast cancer diagnosis occurs in women aged 65 years or older, only 8% of patients in the trial were in this age group.

In summary, older patients in fair to good health tolerate standard and intensive chemotherapy regimens almost as well as younger patients. The authors note that older patients with high-risk early breast cancer who are otherwise in good health should be offered participation in clinical trials of adjuvant chemotherapy.

Original article Muss HB *et al.* (2005) Adjuvant chemotherapy in older and younger women with lymph node–positive breast cancer. *JAMA* **293:** 1073–1081

Alternative splicing of *KLF6* associated with increased risk of prostate cancer

One of the strongest risk factors for prostate cancer is family history of disease, but the predisposing genetic factors are unknown. KLF6 suppresses cell growth through p53-independent transactivation of p21, and mutations leading to the inactivation or loss of KLF6 have been linked to other human cancers. Narla *et al.* investigated the possibility that inherited *KLF6* mutations or polymorphisms exist that may increase prostate cancer risk.

Direct sequencing of genomic DNA isolated from blood revealed one very frequent polymorphism, *IVSΔA*; IVS1–27 G > A. To identify a possible association between this single nucleotide polymorphism and prostate cancer risk, germline DNA was genotyped from 3,411 geographically diverse men from three independent institutions, including 1,253 sporadic cancer patients, 882 familial cancer patients and 1,276 control men. It was found that there was a significant association between *IVSΔA* and cancer in both sporadic and familial cancer.

Using *KLF6* minigene constructs in cultured cells, it was established that *KLF6* was alternatively spliced, that there was an overabundance of *KLF6* splice variants to wild type in tumor tissue, and that IVSΔA was consistently associated with enhanced *KLF6* alternative splicing and variant protein expression. Complementary DNA sequence analysis confirmed the presence of three alternatively spliced *KLF6* gene transcripts. These findings led to the suggestion that *IVSΔA* effected a change in wild-type *KLF6* tumor suppressor gene expression and function. A splicing enhancer motif prediction program showed that the *IVSΔA* allele generates a functional SRp40 binding sequence, and studies with minigene constructs showed that spliced forms of KLF6 antagonize wild-type KLF6 effects on p21 and cell growth.

The authors note that the critical balance between the growth-suppressive and growth-promoting forms of KLF6 can profoundly influence prostate biology and cancer risk.

Original article Narla G *et al.* (2005) A germline DNA polymorphism enhances alternative splicing of the *KLF6* tumor suppressor gene and is associated with increased prostate cancer risk. *Cancer Res* **65:** 1213–1222

Localized aggressive lymphoma: ACVBP compared with CHOP plus radiotherapy

A chemotherapy regimen comprising an induction phase of intensified doxorubicin, cyclophosphamide, vindesine, bleomycin and prednisone (ACVBP), with subsequent sequential consolidation, has been developed as a new treatment for limited (stage I or II) aggressive lymphoma, in place of the standard chemoradiotherapy treatment. In a previous study, the estimated 5-year rate of overall survival with this treatment regimen was comparable for intermediate and high-grade lymphoma with that found in other trials using chemoradiotherapy.

This randomized trial compared the ACVBP regimen with chemoradiotherapy for 647 patients aged below 61 years with localized, stage I or II, aggressive lymphoma and no adverse prognostic factors. Chemoradiotherapy