with improved overall survival ($P=0.015$), and a reduction in the occurrence of distant metastases ($P<0.0001$).

The authors conclude that the addition of trastuzumab to an adjuvant chemotherapy regimen comprising doxorubicin and cyclophosphamide followed by paclitaxel significantly improves outcome in this patient population.

Alexandra King

Original articles Piccart-Gebhart MJ *et al.* (2005) Trastuzumab after adjuvant chemotherapy in HER-2 positive breast cancer. *N Engl J Med* 353: 1659–1672
Romond EH *et al.* (2005) Trastuzumab plus adjuvant chemotherapy for operable HER-2 positive breast cancer. *N Engl J Med* 353: 1673–1684

Predicting mortality after hormonal therapy for postsurgical or postradiologic PSA failure

Around 30% of patients with localized prostate cancer who undergo radical prostatectomy or external-beam radiation therapy show PSA failure within 10 years and median survival in these patients is related to PSA doubling time. PSA doubling time prior to the initiation of primary androgen-suppression therapy (AST) has also been associated with prostate-cancer-specific mortality (PCSM), as has posthormonal PSA nadir. Although it has been shown that patients who do not achieve a post-AST nadir below 0.2 ng/ml following primary treatment have an increased risk of PCSM, it is not known whether this also applies in cases of secondary AST given for PSA failure after surgery or radiation therapy.

In this study of 747 men with rising PSA and negative bone scans after radical prostatectomy ($n=486$) or external-beam radiation therapy ($n=261$), PSA nadir at 8 months post-AST initiation, pre-AST PSA doubling time, PSA level and a Gleason score of 8–10 were significantly associated with time to PCSM. A PSA nadir of >0.2 mg/ml combined with pre-AST PSA doubling time of <3 months was closely associated with PCSM, independent of initial prostate cancer treatment, and this profile was seen in 75% of those patients who died of prostate cancer over the observation period of the study. Given the clinical relevance of these findings, the authors suggest that

these criteria are a useful endpoint for future clinical trials.

Carol Lovegrove

Original article Stewart AJ *et al.* (2005) Prostate-specific antigen nadir and cancer-specific mortality following hormonal therapy for prostate-specific antigen failure. *J Clin Oncol* 23: 6556–6560

Radiotherapy of left-sided breast cancer does not increase cardiac morbidity

Radiotherapy following breast-conserving surgery improves overall outcomes and decreases the risk of local recurrence; however, left-sided breast irradiation can cause cardiac damage and might be associated with increased risk of cardiac morbidity. The long-term effects of adjuvant breast irradiation are not well defined, and risk assessment based on early studies might not be valid because modern techniques have reduced the radiation dose and the volume of heart tissue exposed to radiation.

Patt *et al.* followed women with nonmetastatic breast cancer (8,363 left-sided and 7,907 right-sided) who had received adjuvant radiotherapy between 1986 and 1993. Cox's proportional hazards model was used to compare the incidence of hospitalization caused by ischemic heart disease, valvular heart disease, conduction abnormalities, or cardiomyopathy or heart failure in women with left-sided versus those with right-sided cancer. After a mean follow-up of 9.5 years, there was no significant difference in the rates of hospitalization for cardiac events between women treated with radiotherapy for left-sided and those treated for right-sided breast cancer. The risk of ischemic heart disease increases with time; however, in an additional analysis with 10–15 years of follow-up, there was no difference in left-sided versus right-sided breast cancer.

In summary, the data suggest that modern adjuvant radiotherapy does not cause significant cardiovascular disease. Nevertheless, there is a strong correlation between doses of radiation to the myocardium and risk of death from cardiac events; therefore, additional reductions in myocardial radiation are likely to be beneficial.

Kate Matthews

Original article Patt DA *et al.* (2005) Cardiac morbidity of adjuvant radiotherapy for breast cancer. *J Clin Oncol* 23: 7475–7482