prior radiotherapy and the number of metastatic sites (none or one vs two or three) were also independent predictors of survival. The main effect of adding these two additional factors to the model was to reclassify some of the 'intermediate risk' patients into the favorable or poor-risk groups.

In conclusion, this study validates and extends the model proposed by Motzer *et al.* An international consortium has now been set up to continue the work and to agree a common approach.

Original article Mekhail TM *et al.* (2005) Validation and extension of the Memorial Sloan-Kettering prognostic factors model for survival in patients with previously untreated metastatic renal cell carcinoma. *J Clin Oncol* **23:** 832–841

Radioimmunotherapy for follicular lymphoma

The radioimmunoconjugate ^{131}I-tositumomab has shown promise in the treatment of recurrent follicular lymphoma. For the first time, Kaminski *et al.* have used the drug in previously untreated patients.

This phase II, open-label study included 76 consecutive patients with low-grade, B-cell lymphoma. All had stable or progressive disease and had received no previous treatment. Patients received a single course of ^{131}I-tositumomab therapy and were followed up for a median period of 5.1 years. A response was observed in 72 (95%) patients; regression of the palpable tumor was in most cases noted within 2 weeks. A complete response—defined as the disappearance of all disease for 1 month or more, or no change in minimal residual radiographic abnormalities for at least 6 months—was recorded in 57 (75%) patients, within a median time of 202 days. Forty of these complete responders remained in remission for 4.3–7.7 years. These response rates were higher than have been achieved using this therapy in previously treated patients. Hematologic toxicity was moderate and reversible, and no patient developed acute myeloid leukemia or myelodysplastic syndrome.

In an accompanying editorial, Joseph Connors points out that the patients included in this study had a good prognostic profile. They had slowly progressive disease, were younger than the average patient and had lower tumor burden. He notes that, while the results were impressive, randomized trials will be needed to determine whether the treatment is superior to current strategies.

Original article Kaminski MS *et al.* (2005) ^{131}I-tositumomab therapy as initial treatment for follicular lymphoma. *New Engl J Med* **352:** 441–449

Gene-expression profiling to predict cancer outcome

Gene-expression profiling aims to classify patients according to a 'molecular signature' derived from microarray analysis. In the field of oncology, this approach promises to identify genes that are differentially expressed in tumors with different outcomes. Treatment strategies can then be tailored to the patient, based on the gene-expression profile.

This type of analysis involves large amounts of data and several possible methods for classifying patients, so it is possible that some findings are not robust. Michiels and co-workers reanalyzed data from the seven largest studies in this area and concluded that 'the prognostic value of published microarray results in cancer studies should be considered with caution'.

Each study included at least 60 patients and provided data on disease-free, event-free or overall survival. Using data from multiple, random sets of patients derived from the original training and validation sets, Michiels *et al.* examined the stability of the molecular signature and the extent to which patients were misclassified. In each case, they defined 'favorable' and 'unfavorable' expression profiles based on the 50 signature genes for which expression most closely predicted outcome.

The molecular signature was highly unstable; the list of genes that appeared to predict outcome varied greatly, depending on which patients were included in the training sets. In five of the seven studies, classification of patients was no more accurate than would have been expected by chance. Michiels *et al.* recommend that future studies should include larger sample sizes and use repeated random sampling for validation.

Original article Michiels S *et al.* (2005) Prediction of cancer outcome with microarrays: a multiple random validation strategy. *Lancet* **365:** 488–492