dose density was significantly associated with progression-free survival ($P = 0.003$). Notably, neither the Memorial Sloan–Kettering Cancer Center criteria nor the Medical Research Council criteria for relapsed GCT were able to identify a poor-prognostic group for GAMEC.

The authors conclude that GAMEC is an effective treatment for patients with untreated or relapsed GCT, although it results in substantial toxic effects.

**Original article** Shamash J *et al.* (2007) GAMEC—a new intensive protocol for untreated poor prognosis and relapsed or refractory germ cell tumours. *Br J Cancer* **97:** 308–314

## Short-term use of rofecoxib increases the risk for adverse cardiovascular events

Inhibition of cyclo-oxygenase 2 might slow the progression of colorectal cancer, but might also increase the risk of adverse cardiovascular events. The cyclo-oxygenase 2 inhibitor rofecoxib was withdrawn worldwide in 2004 after a large trial demonstrated that patients receiving this drug were at an elevated risk of cardiovascular thrombotic events. Kerr *et al.* have now analyzed data from the VICTOR trial of rofecoxib in patients who had undergone curative surgery for colorectal cancer in order to evaluate the cardiovascular risks associated with the short-term use of this drug to prevent disease recurrence. Patients were randomized to receive either 25 mg/day rofecoxib or placebo.

The VICTOR trial was prematurely stopped after the withdrawal of rofecoxib, with a total of 2,434 patients having been recruited. The median duration of treatment was 7.4 months for the rofecoxib group and 8.2 months in the placebo group. Median durations of follow-up were 33.0 and 33.4 months, respectively. After adjustment for cardiovascular risk factors, the relative risk of a cardiovascular thrombotic event occurring during treatment or within 14 days after termination of treatment was 2.41 (95% CI 0.93–6.26) for the rofecoxib group (16 events) compared with the placebo group (7 events). During the treatment phase and a 2-year follow-up period, the unadjusted relative risk for a cardiovascular thrombotic event was 1.50 (95% CI 0.76–2.94) for the rofecoxib group compared with the placebo group.

The authors conclude that even short-term (<18 months) use of rofecoxib is associated with increased risk for a cardiovascular thrombotic event.

**Original article** Kerr DJ *et al.* (2007) Rofecoxib and cardiovascular adverse events in adjuvant treatment of colorectal cancer. *N Engl J Med* **357:** 360–369

## Prognostic factors in patients with metastatic RCC receiving anti-VEGF therapy

Current treatment algorithms for patients with advanced renal cell carcinoma (RCC) were developed on the basis of patients treated with cytokines or chemotherapy; however, most patients now receive VEGF-targeted therapies. Choueiri *et al.* have identified five factors that can predict progression-free survival (PFS) in patients treated with anti-VEGF agents and used these factors to develop a prognostic model.

Data were reviewed for 120 patients with metastatic clear-cell RCC enrolled into one of the two compassionate-use studies or nine prospective trials conducted at the Cleveland Clinic Taussig Cancer Center, OH, between October 2003 and January 2006. These patients were treated with the anti-VEGF agents bevacizumab, sunitinib, sorafenib or axitinib, and no patient had previously received anti-VEGF therapy. Overall estimated median PFS was 13.8 months, and 34% of patients achieved an objective response according to the RECIST criteria. Through multivariate analysis, the following factors were identified and validated as independent adverse prognostic indicators of PFS: <2-year interval between diagnosis and current treatment; baseline platelet count $>300 \times 10^9$/l; baseline neutrophils $>4.5 \times 10^9$/l; baseline corrected serum calcium <8.5 mg/dl or >10 mg/dl (<2.1 mmol/l or >2.5 mmol/l); and initial ECOG performance status ≥1. These adverse prognostic factors were used to define three prognostic subgroups. Median PFS was 20.1 months in patients with 0–1 factor, 13 months in those with 2 factors, and only 3.9 months in those with >2 factors.

These prognostic factors can, say the authors, be easily incorporated into patient care and stratification schema for future clinical trials of novel, VEGF-targeted agents.

**Original article** Choueiri TK *et al.* (2007) Clinical factors associated with outcome in patients with metastatic clear-cell renal cell carcinoma treated with vascular endothelial growth factor-targeted therapy. *Cancer* **110:** 543–550