Long-term neurotoxic and ototoxic effects were associated with carboplatin.

The authors conclude that patients with GCTs and a poor predicted outcome to conventional carboplatin-based salvage chemotherapy can benefit from TICE salvage chemotherapy plus stem-cell support. To minimize ototoxic effects, the authors suggest that aminoglycosides are avoided after high-dose carboplatin.

Original article Kondagunta GV *et al.* (2007) Paclitaxel plus ifosfamide followed by high-dose carboplatin plus etoposide in previously treated germ cell tumors. *J Clin Oncol* **25:** 85–90

Sorafenib prolongs survival in patients with advanced RCC

Systemic therapies for patients with renal cell carcinoma (RCC) include high-dose interleukin 2 and interferon α; however, these cytokines rarely induce complete response or prolonged survival and are not always well tolerated. Sorafenib, a multiprotein kinase inhibitor, has been shown to have antitumor activity in renal adenocarcinoma animal models and to prolong survival in patients with metastatic RCC. In a phase III trial, Escudier *et al.* showed that sorafenib prolonged survival in patients with advanced clear-cell RCC in whom previous therapy had failed.

The study included 903 patients (aged ≥18 years) with clear-cell RCC who were randomly assigned to receive either placebo (arm A) or 400 mg oral sorafenib twice daily (arm B). Both groups had similar baseline characteristics and the majority of participants had previously received cytokine-based therapy and had undergone nephrectomy. The average overall survival rates for patients in arm A and arm B were 15.9 and 19.3 months, respectively ($P = 0.02$). Progression-free survival was also significantly extended after sorafenib treatment (5.5 months versus 2.8 months; $P < 0.001$). The percentage of patients with partial response or stable disease was higher in the sorafenib-treated group than in the placebo group (10% versus 2% and 74% versus 53%, respectively; $P < 0.001$). The most frequent adverse events in the sorafenib-treated group were diarrhea, rash, fatigue, hand–foot skin reactions, alopecia, and nausea; cardiac ischemia and hypertension were also observed.

The authors conclude that oral sorafenib therapy prolongs progression-free survival in the subset of patients with advanced clear-cell RCC who do not respond to first-line therapy.

Original article Escudier B *et al.* (2007) Sorafenib in advanced clear-cell renal-cell carcinoma. *N Engl J Med* **356:** 125–134

Sunitinib improves response and survival rates in metastatic RCC

Patients with metastatic renal cell carcinoma (RCC) have low rates of response (5–20%) to first-line therapy with interleukin 2 or interferon α; median overall survival is approximately 12 months. The multityrosine kinase inhibitor sunitinib malate targets the overexpression of vascular endothelial growth factor receptor (VEGFR) and platelet-derived growth factor receptor (PDGFR) that occurs in many cases of RCC through inactivation of the *VHL* gene, and has shown promise in cytokine-resistant patients. Data from a phase III trial provide further evidence that angiogenic inhibition is promising as a treatment strategy for clear-cell RCC.

Motzer *et al.* randomized 750 patients with metastatic clear-cell RCC to first-line treatment with sunitinib (50 mg orally once daily for 4 weeks, then 2 weeks without treatment, in 6-week cycles) or interferon α (titrated to 9 MU subcutaneously 3 times a week). Patients in the sunitinib group had significantly longer median progression-free survival than those on interferon α (11 vs 5 months; $P < 0.001$). Sunitinib also resulted in a significantly increased objective response rate (31% vs 6%; $P < 0.001$). Symptoms including diarrhea and grade 3 or 4 neutropenia were more frequently reported in the sunitinib group, but patients on this treatment reported a significantly better quality of life than did patients on interferon α ($P < 0.001$), and most adverse events resolved upon dose interruption or modification. Long-term data are needed to clarify issues such as the role of angiogenic growth factors in metastatic RCC, and the relative survival benefits of sunitinib and interleukin 2.

Original article Motzer RJ *et al.* (2007) Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med* **356:** 115–124