

of translational repression and/or induction of the different genes varied widely. Global analysis using microarray technology indicated that as many as 5% of all genes may be differentially affected during hypoxia through regulation of mRNA translation.

Scientific Symposium

What is new in renal cancer

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INVITED

Systemic therapy and novel targeted therapies in renal cancer

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Renal cell carcinoma has always been considered a chemo-resistant disease and data from the 1980s suggests that response rates are very low. There have however, only been limited data on the newer cytotoxic agents and more recently, non randomised trials have suggested that some patients may respond to combination treatments such as gemcitabine plus capecitabine. It is becoming increasingly recognised that renal cell carcinoma is not a single disease entity. Histology subtype and specific molecular abnormalities may not only define the behaviour of individual tumours but may also have therapeutic relevance. This is best exemplified in relation to targeted therapies. Hormone treatments have for many years been used as second-line treatment in patients who have failed first-line immunotherapy or as initial therapy in those unfit for immunotherapy. They are associated with low response rates and randomised trials suggest that at least, at first-line these treatments confer little or no benefit.

Standard therapy involves immunotherapy with either interferon or interleukin 2. There are randomised data that support the use of interferon and non-randomised data that suggest high dose bolus interleukin 2 is associated with durable complete remissions in a small percentage of patients. There is no evidence that combination immunotherapy is associated with an overall survival benefit. Case-controlled studies and a recent randomised trial from the French cooperative group show that immunotherapy is of no benefit to patients with intermediate or poor prognosis disease.

There is something of a revolution taking place in the treatment of renal cell carcinoma and a number of new targeted agents have shown activity in this disease. The most notable activity and best data produced so far involves Sutent and Sorafenib, the multi targeted tyrosine kinase inhibitors and Avastin, the monoclonal antibody directed against VEGF.

Sutent has shown response rates of nearly 40% in two consecutive phase 2 trials. These studies have involved 160 patients and this makes these data of great interest. Similarly, Sorafenib has shown significant activity in second-line with a doubling of progression-free survival. These are particularly impressive data as the trial was randomised; patients with stable or responding disease were randomised to continue on Sorafenib or placebo. Avastin has an overall response rate of 10% and at higher doses, a statistically significant prolongation of progression-free survival in a randomised trial against placebo. Other targeted agents that have shown activity include Temsirolimus and infliximab.

Trials in the first-line setting are currently underway with Sutent, Sorafenib and Temsirolimus being compared to interferon. Avastin has been combined with interferon and is being compared to single agent interferon. These agents and other targeted compounds are being combined and further data are awaited. Within the next 12–24 months we will have a clearer picture of the precise efficacy of these novel agents, particularly in comparison to interferon. Positive results from these studies will beg many questions: will these new agents replace interferon or will they be given in combination with it? Which targeted agents should be combined and will that be a better strategy than administering them sequentially? Do these compounds with their relatively good toxicity profile, open up therapeutic options for those patients with poor prognostic features who are currently considered unfit for active treatment? Can we now start developing maintenance strategies? We are entering a new therapeutic era in renal cell carcinoma and it is imperative that we now conduct a series of well-designed trials to precisely define how these new compounds can best be utilised.

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Scientific Symposium

Laparoscopic surgery versus conventional surgery in colorectal cancer

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INVITED

Laparoscopic versus open surgery for colon cancer: short-term outcomes of a randomised trial – COLOR Trial

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Background: Oncological safety and short term benefits of laparoscopic colectomy for cancer remain under debate. To investigate these outcomes, a multicenter study randomizing patients with colonic cancer for either laparoscopic or open resection was performed.

Patients & Methods: Twenty-nine European hospitals participated in the COLon cancer Laparoscopic or Open Resection trial (COLOR trial). Patients with a solitary cancer of the right or left colon were randomly assigned to either laparoscopic or open surgery as curative treatment. Cancer free survival at three years after surgery was the primary outcome. Clinical characteristics, operative findings and postoperative outcome are presented.

Results: Of the 1248 patients randomly assigned to one of the two surgical procedures, 153 were excluded and 13 could not be analyzed due to missing data.

Blood loss was significantly less during laparoscopic than during open surgery ($p < 0.001$). Laparoscopic surgery took half an hour longer to perform than open surgery ($p < 0.001$). In 17% of the laparoscopic procedures conversion to open resection was necessary. Radicality of resection assessed by number of removed lymph nodes and length of resected oral and aboral bowel segments was similar after laparoscopic and open surgery. During the postoperative course, laparoscopic colectomy was associated with earlier recovery of bowel function ($p < 0.001$), fewer analgesics requirements ($p < 0.001$) and one day shorter hospital stay ($p < 0.001$). Rates of morbidity and mortality within 28 days after colectomy did not differ between arms.

Interpretation: Laparoscopic surgery allows safe and radical resection of colonic cancer of the right, left and sigmoid colon. Although laparoscopic colectomy requires more operating time, it is associated with less blood loss, earlier restoration of bowel function, fewer analgesic requirements and shorter hospital stay.

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The CLASICC trial

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The CLASICC Trial is a randomised clinical trial of laparoscopic-assisted versus conventional surgery in colorectal cancer. Between 1996 and 2002 794 patients from 27 UK centres were allocated to undergo laparoscopic-assisted ($n = 526$) or open ($n = 268$) surgery for cancer of the colon ($n = 413$) or rectum ($n = 381$). All surgical resection specimens were treated identically and centrally reviewed for circumferential resection margins (CRM) positivity. In the lap-assisted group overall 29% underwent conversion to open surgery but this fell from 38% in year 1 to 16% in year 6 of the trial. Tumour stage was equivalent between the two arms of the trial and the proportions of Dukes stage C₂ tumours did not differ between the lap-assisted (7%) and open (6%) groups. Duration of operation was shorter in the open (135 [100–180] min) than in the lap-assisted (180 [135–220] min) group. Rates of CRM positivity were similar between groups except for those undergoing laparoscopic anterior resection for rectal cancer where CRM positivity was 12% ($^{16}/_{126}$) compared with 6% ($^{4}/_{64}$) in the group undergoing open anterior resection ($p = 0.19$). Lymph node yield was high in both arms (13.5 open, 12 lap-assisted). In the lap-assisted group average hospital stay was 2 days shorter than in the open group. Overall 30-day complication rates were identical in the two arms but in those who underwent conversion from laparoscopic to open surgery the complication rates were higher and this was reflected in a higher in-hospital mortality (open 5%, lap-assisted 1%, converted 9%, $p = 0.34$). Up to 3 months postoperatively quality of life scores (EORTC QLQ-C30, and QLQ-CR38) showed similar patterns between the two surgical groups. All patients have now been followed up for at least 3 years.

For cancer of the colon there seems to be little difference between laparoscopic-assisted and open resection and on the basis of the pathological data there is no reason to suspect that cancer-related outcomes will be different. Preliminary analysis of the 3-year overall and disease free survival bears this out. For rectal cancer the data might suggest that a higher local recurrence rate might be expected in those