WEDNESDAY 24 OCTOBER 2001

Teaching Lectures

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Novel methods in cervical cancer screening

Abstract not received.

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Progress made in ovarian cancer treatment

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Ovarian cancer is the most lethal of the gynaecological cancers; the majority of patients die of disease because in most cases it is disseminated beyond the ovary (Stage III or IV) at diagnosis. What progress has been made in it's management over the past 10 years?

(a) For the majority of patients with true Stage I disease, the role of adjuvant chemotherapy is still uncertain. A recent large scale randomized trial (ICON-1, ACTION) did demonstrate a difference in favour of adjuvant platinum-based chemotherapy (7% increase in 5 year survival), but this may in part have related to surgical understaging of disease.

(b) For the majority of patients with Stage III and IV disease, many clinicians agree that standard treatment should comprise 6 cycles of paclitaxel-carboplatin. Randomized trials over the past 10 years have indicated the superiority of paclitaxel-based treatment and that carboplatin is equivalent to cisplatin but much better tolerated. A recent trial has also suggested that docetaxel may be a better option than paclitaxel, because of reduced neurotoxicity and comparable efficacy. However, treatment results remain unsatisfactory, since the median survival for these patients is still only 2–3 years. Future progress may be made by addressing the following issues:

- Would sequential regimens be more effective? Intriguing results from 2 large randomized trials (ICON-3 and GOG-32) indicate that single agent platinum might well be incorporated into such regimens. In addition a range of other agents could be tested as part of first line regimens, having demonstrated activity in the relapse setting. These include topotecan, gemcitabine and Caelyx.
- Could results be improved by incorporating a cell signalling inhibitor, e.g. ZD1839, the EGFr tyrosine kinase inhibitor? These drugs have potential as single agents, but may be particularly effective in combination with current drugs.

Real progress can be expected when a better understanding is achieved of the mechanisms underlying clinical drug resistance in ovarian cancer, and a close laboratory-clinical interaction is crucial.

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Optimal radiotherapy in head and neck tumours: from biology to physics

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Based on personal experience and through a review of the literature concentrated on major trials dealing with altered fractionation, this lecture will be aimed at (a) emphasizing the common denominators and discrepancies existing among the results observed for various categories of altered fractionation regimes and (b) identifying the potential interactions between patient- and tumor-related factors on the one side, and treatment parameters on the other side that might influence the disease outcome when the fractionation is altered.

In particular, differences in acute and late effect patterns following hyperfractionated and accelerated regimes (HF, AF) of radiotherapy will be analysed. Moreover, the fact that in practically all studies on accelerated fractionation, in which a compromise was made on total dose (namely, <60 Gy), no benefit was elicited in favour of the experimental arms, regarding LR control or DFS will be revisited. Whether AF and HF regimes be applied on an invidual basis only will also be discussed through a critical appraisal of the use of predictive tests (fast growing tumors: AF?; high intrinsic radio-resistance, tumor differentiation: HF?).

On the other hand, as regards the use of modifiers of radioresponsiveness, novel approaches which are currently under investigations, will be reviewed. As for cytotoxic drugs, phase III studies are studying the impact of combinations of RT with mono- or polyagent schedules based on CDDP, 5-FU, or Mitomycin C, whilst phase I-II studies are directed to the concurrent delivery of Taxanes, Gemcitabine, Tirapazamine, Porphyromycin, or other bioreductive drugs. Likewise, non cytotoxic drugs are tested in the framework of Phase I or II studies: Ad5p53, EGFR-Mab, inhibitors of farnesyl transferase, or amifostine, as radioprotector for normal tissues. The potential role of Erythropoietin in anemic patients will also be reviewed, as well as the future translational research targets which should include DNA repair or cell cycle regulation proteins, apoptosis, angiogenesis, and signal transduction pathways.

Finally, the perspectives offered by three-dimensional conformal radiotherapy and techniques of intensity modulation will be extensively presented, especially as regards their impact on disease outcome and quality of life.

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Criteria for optimal surgery in gastrointestinal cancer

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Safety, radicality and long term outcome are important criteria in gastrointestinal cancer surgery. Developments in pancreatic and rectal cancer treatment will illustrate how results can be optimised. Advances in the operative and perioperative management of cancer patients and the formation of specialized centers have contributed to a significant decrease in mortality and morbidity. The adequacy of cancer resection, assessed by the R-classification(R0-R2), depends on local tumour extension and spread and on adequate surgical technique. The safety of cancer surgery, however, is predominantly associated with reliable reconstructive techniques and early management of postoperative complications.

In pancreatic surgery the mortality has decreased and is <5% for the majority of tertiary referral centers. Mortality is more often caused by systemic co-morbidity than by surgical complications. Total morbidity ranges from 20 to 40% and includes delayed gastric emptying after pancreatoduodenectomy in 20 to 30% of patients as the most prevalent complication. The extent of adequate lymph node dissection in pancreatic cancer resection is still debated and results of further randomised controlled trials are awaited. Five year survival after radical surgery for pancreatic ductal adenocarcinoma is 10 to 30% (24% in our own institution) and a recent randomised controlled trial (ESPAC-1) demonstrated that adjuvant chemotherapy improves survival.

In rectal cancer surgery total mesorectal excision according to Heald has dramatically improved the outcome. Total mesorectal excision is technically demanding and the criteria for optimal surgery are the virtual elimination of local recurrences (<5%) and the preservation of pelvic nerves to reduce postoperative urogenital dysfunctions. Treatment strategies that include neoadjuvant chemo-radiation are valuable in patients with locally advanced tumours. Despite more radical resections, continence preserving procedures are generally possible except for patients presenting with tumours that infiltrate the anal sphincter. Functional results after rectal cancer surgery depend on the formation of neorectal reservoirs, including the standard Colon J-Pouch and the more recently developed Transverse Coloplasty Pouch.

In conclusion, criteria for optimal surgery in gastrointestinal cancer can often be defined and should be included in gastrointestinal cancer treatment strategies.