front-line strategies for high risk patients, if proven useful in the ongoing randomized clinical trials
(2) Some new "predictive" molecular markers will hopefully assist the medical oncologist in selecting patients who need aggressive therapies
(3) Some of the studies that currently evaluate the clinical potential of new agents, such as pure antioestrogens, liarozole, Capecitabine, Caelyx, Gemcitabine ... will clarify their role in the management of breast cancer
(4) Entirely new therapies, interfering with signal transduction or angiogenesis pathways will be assessed as an adjunct to chemotherapy and hormonal therapy

All these innovative drugs or strategies will be discussed.

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A randomized single-institution study of high-dose chemotherapy with cyclophosphamide, thiotepa and carboplatin (CTC) in apical node-positive breast cancer

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Between May 1991 and December 1995, 97 patients were included in a study of high-dose chemotherapy (CTC) in stage II or III breast cancer. All patients were below 60 years and had a tumor-positive apical axillary lymph node at infraclavicular biopsy. The conservative treatment arm consisted of 3 courses of FEC: fluorouracil (500 mg/m^2), epirubicin (120 mg/m^2) and cyclophosphamide (500 mg/m^2). Responders were randomized and went on to definitive surgery, a fourth course of FEC, radiation therapy and two years of tamoxifen. Patients in the experimental arm additionally underwent high-dose chemotherapy with cyclophosphamide (6 g/m^2), thiotepa (480 mg/m^2) and carboplatin (1600 mg/m^2), followed by blood progenitor cell (PBPC) transplantation after FEC-4. Eighty-one patients were randomized: 40 to undergo conventional treatment only and 41 to receive CTC + PBPC transplantation. With a median follow-up of 42 months, the progression-free survival for all patients was superior to historical controls, but the curves of the two treatment arms are superimposable. Evidence from randomized studies is urgently required to establish the value of high-dose therapy in the treatment high-risk breast cancer.

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Models of environmental effects on intestinal tumour development

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Purpose: Germ-free conditions can abrogate cellular proliferative effects of diets in mice, hence differing environments might affect spontaneous tumour development *in vivo* and can be studied in the "Multiple intestinal neoplasia" (MIN) mouse.

Methods: MIN carries a nonsense mutation in the mouse *Apc* gene, the earliest genetic defect in sporadic colon tumours. Heterozygous mice develop multiple polyps by 60 days of age. Mice were reared in conventional microbiological (two different diets), Specified Pathogen Free (SPF) and totally germ free environments. They were deemed ill for sacrifice independently of tumour assessments which were done blind. The small intestine was sub-divided into equal thirds and the polyps counted and measured under a X10 dissecting microscope.

Results: SPF Mice have higher small and large bowel intestinal tumour counts (mean ± SEM: conventional 21.4 ± 1.25 & 1.8 ± 0.21 *Vs* SPF: 33 ± 1.27** & 3.6 ± 0.32** respectively), which also reflected in their reduced survival (231.3 ± 9.5 *Vs 184.3 ± 5.0* days**). The terminal ileum accounted for the majority of the small bowel effect. Effects of dietary Fat showed similar increases in tumour number and also caused tumour enlargement. To date (n = 5) in totally germ-free MIN, there has been complete suppression of colonic tumour formation with no obvious small bowel effects. **$P < 0.01$.

Conclusions: The micro-environment can be manipulated both by microbiological and dietary means with powerful influences on early colonic tumour development. These effects will be discussed in the context of other micro-environmental modifiers which may lead to novel therapeutic approaches.

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Hereditary nonpolyposis colorectal cancer is preventable

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The claim that these cancers are preventable, or at least detectable at an early stage, stems from a 10 year clinical screening program in which mortality from cancer was significantly reduced in members of hereditary nonpolyposis colorectal cancer (HNPCC) families who are at 50% genetic risk of being carriers of predisposing gene mutations (Järvinen et al. *Gastroenterology* 1995). Clinical screening and preventive measures should ideally be offered only to those family members who are mutation positive and avoided in those who are negative. This can now be accomplished through efficient mutation detection. Thus cancer prevention can be accomplished in *known* HNPCC families. However, a major challenge is that most HNPCC cases are presently undiagnosed. In this presentation a strategy is proposed by which patients newly diagnosed with colorectal or other HNPCC cancers can be relatively efficiently and reliably screened for HNPCC. In a pilot study of 500 such patients, 10 new cases of HNPCC (2%) were diagnosed in this way. These developments raise the possibility that, under certain general conditions, all newly diagnosed "sporadic" patients can be molecularly screened for HNPCC.

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Epidemiology and screening of colorectal cancer

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Colorectal cancer is one of the most frequent cancers. It has been estimated in the European Union that the number of new cases was 135,000 each year. This cancer is unequally spread geographically, and is among the most frequent in Western Europe and North America. Considering the present state of knowledge, only the strategy of screening for intestinal tumours at their asymptomatic stage could reduce a problem such as colorectal cancer. Data from case-control studies provides evidence of the efficacy of screening by rigid proctosigmoidoscopy or colonoscopy. The effectiveness of screening with endoscopy has yet to be demonstrated. Compliance with such a strategy is not known. Case-control studies and randomised studies indicate that it is possible to reduce mortality from colorectal cancer in people who accept screening with faecal occult blood testing. Population-based studies rely on a biennial Hemoccult test. To be effective on colorectal cancer mortality compliance has to be between 55% and 65% in the first screening campaign, and to remain high in the succeeding ones. It has also been shown that the colorectal cancer screening strategy meets commonly accepted criteria for cost-effectiveness. The time has come to encourage colorectal cancer screening with faecal occult blood test despite the current limitations of available tests.

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Staging and treatment of early rectal cancer

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Improved understanding of the biological features of rectal cancer and advances in diagnostic and surgical procedures result in an increased number of sphincter preserving operations in lower rectal tumors. The relevant diagnostic and treatment strategies along with their indications will be presented and analyzed.

New methods in preoperative staging with the use of three-dimensional endorectal ultrasonography which provides previously unattainable scan plans, the high-resolution magnetic resonance tomography by using an endorectal coil and the 3-D multi tissue CT-reconstruction enables the visualization of local tumor spread. These techniques improve therapy planning in rectal cancer by selecting patients for alternative therapeutical methods.

New local surgical techniques including transanal endoscopic microsurgery have been proven to fulfill radical oncologic guidelines for patients with early rectal cancer (uT1-2, G1-2).

Among the radical approaches an ultralow anterior rectal resection with colon-pouch creation and a coloendoanal anastomosis make it possible to extend the resection line to the ano-rectal junction without loss of continence.

Recently, a continent perineal colostomy has been developed. This technique can be used in cases where the removal of the rectal sphincter is