Conclusions: Adjuvant CHTH in urothelial cancer of urinary tract isn't a standard treatment. Half of pts treated with adjuvant CHTH relapsed in one year. The risk of relapse remained comparable with results obtained in pts without adjuvant treatment. The optimal strategy of management in this high-risk pts is to be defined in prospective way.

901 POSTER

Effective first-line chemotherapy with docetaxel and gemcitabine in advanced bladder cancer (ABC)

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Background: Docetaxel and gemcitabine are two promising drugs in ABC, yielding high response rates as monotherapy with manageable toxicity. Moreover, there is evidence of synergism between docetaxel and gemcitabine in various tumours.

Materials and methods: Twenty-one patients (16 male, 5 female) with stage IV ABC have been enrolled. Aged 42-73 (median 63) years, ECOG PS 0-2, 6 and 7 patients had been treated with adjuvant chemotherapy and radiotherapy, respectively. Treatment consisted of docetaxel 75 mg/m^2 d1 as a 60-min iv infusion after standard premedication and gemcitabine 1000 mg/m^2 dl + d8 as a 30-min iv infusion, repeated every 3 weeks for up to 6 cycles.

Results: A total of 105 cycles have been administered (median 5/patient). Grade 3-4 haematological toxicities included neutropenia 20%, thrombocytopenia 10%, and anaemia 10%, with febrile neutropenia in 4 patients and 9 cycles. G-CSF and EPO were judged necessary in 11 and 5 patients, respectively. Treatment delay was required in 5 patients and 7 cycles. No toxic deaths occurred. Haematological toxicity was generally manageable and as seen in other studies with the two agents (alopecia, asthenia, serious onycholysis, diarrhoea, mucositis, dyspnoea). Thirteen patients responded clinically and/or radiologically with 3 complete responses (2 liver metastases); 5 patients had stable disease. Median time to progression exceeds 6 months.

Conclusion: Preliminary results suggest that the docetaxel-gemcitabine combination is effective and well tolerated in ABC. The study is ongoing.

902 POSTER

Nonseminomatous germ cell testicular tumors clinical stage I: a retrospective analysis.

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The cure rate for nonseminomatous germ cell testicular tumors (NSGCTT) clinical stage I is very high (99%). This can be achieved by different therapeutic strategies. We analyzed retrospectively 100 patients (pts) followed by 2 institutions: 42 accepted and entered into a surveillance program (SP), 58 were treated with retroperitoneal lymph node dissection (RPLND). Patients had either normal serum markers or declining at half-life. Patients characteristics were: median age 28 years (range 16-71) for SP and 28 (range 17-54) for RPLND; embryonal carcinoma component was predominant in 72.5% (SP) and 56% (RPLND pts); vascular invasion was present in 21.4% (SP) and 25% (RPLND pts); serum tumor markers were elevated in 74% (SP) and 47% (RPLND) of cases before orchiectomy; pathological stage II, after RPLND, were revealed in 7 pts. Median follow-up was 9.8 years (9- 250 months) for SP and 8.3 (15-323 months) for RPLND respectively. Relapses were as follow: 14 (33.3%) for SP and 8 (14%) for RPLND; all were treated with cisplatin-based chemotherapy and surgery of residual masses. In the first group sites of relapses were: retroperitoneum (6 pts), lung (2), retroperitoneum and lung (1), mediastinal and retroperitoneal lymph nodes (1); four pts had only an increase of serum tumor markers. Relapses after RPLND were: lung (3), retroperitoneum (2), inguinal lymph nodes (1), retroperitoneum and lung (1), lung retroperitoneal and mediastinal lymph nodes (1). Median time to relapse (TTR) was 6 months (range 2-19) for SP and 4 (2-19) for RPLND. None of the prognostic factors studied (age, tumor size, pathological stage, histology, vascular invasion and serum tumor markers) was predictive of relapse, neither for SP nor for RPLND. In each group the disease specific survival was 100%: one patient died for HIV-related causes in the SP group, and one patient died for car accident 3 years after RPLND. There is only one patient, followed initially with the SP, alive with disease.

Conclusions: i) both strategies allow an optimal cure rate; ii) in each group relapses were observed; iii) median TTR was similar; iv) no prognostic factor examined was predictive of relapse. Therefore, independently from the strategy, an accurate follow-up must be performed for the first 2 years and the patient's choice should be a fundamental point in the decision making.

903 POSTER

Capecitabine-monotherapy and in combination with immunotherapy in the treatment of metastatic renal cell carcinoma

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Purpose: Capecitabine is a novel fluoropyrimidine carbamate, orally administered and selectively activated to fluorouracil by a sequential triple enzyme pathway in liver and tumor cells. This prospective trial aimed to evaluate the therapeutic effects and systemic toxicities of capecitabine monotherapy and capecitabine treatment combined with biological response modifiers in patients with metastatic renal cell carcinoma.

Patients and Methods: 54 patients suffering from metastatic renal cell carcinoma progressing under first-, second-, or third-line treatment entered the trial. Capecitabine was given orally at a dose of 2500 mg/m^2 daily divided into two doses for 14 days, followed by seven days' rest in the monotherapy as well as in the combination treatment. This schedule was repeated in three-week cycles. The combination therapy consisted of capecitabine and an immunotherapy treatment, which consisted either of interferon-gamma 1b (100 mg/d) administered consecutively five times weekly during weeks 1 and 2 and recombinant interleukin-2 (4.5 MU/d) administered on 4 consecutive days during weeks 3 and 4, every 6 weeks, or alpha-interferon (6 MioIE/d) administered three times a week.

Results: 52 patients are now evaluable for response and 54 patients for toxicity. We observed a partial response to treatment in 5 patients (9.6%), minor response in 5 patients (9.6%), stable disease in 32 patients (61.6%), and only 10 patients (19.2%) showed continued disease progression despite treatment. Outpatient capecitabine was well tolerated. We did not observe any WHO-grade IV toxicities.

Conclusion: Capecitabine monotherapy and capecitabine treatment in combination with biological response modifiers appear to be effective regimens with favourable toxicity profiles in patients with advanced renal cell carcinoma. Capecitabine monotherapy seems to be superior than the combination treatment because of its easier application form.

Symptom management/Quality of life

904 POSTER

Health-related quality of life in randomised controlled trials in colorectal cancer.

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Health related quality of life (HRQOL) is an important outcome in clinical trials in colorectal cancer yet there is no established consensus on the methods of optimal measurement of HRQOL for these patients. Recent publications have raised questions regarding the quality of some published health-related quality of life (HRQOL) assessment studies in cancer clinical trials. Hence, t he aim of this systematic review was to evaluate levels of reporting of HRQOL in randomized trials in colorectal cancer.

A comprehensive search from 1980 to March 2003 was performed to identify randomised controlled trials (RCTs) of colorectal cancer patients who had undergone a HRQOL assessment. Articles were identified mainly by MedLine, CancerLit, and the Cochrane Library. All studies enrolling at least 50 patients and using a HRQOL patient self-reported measure were included. Two reviewers (FE & AB), according to a pre-defined-coding scheme, independently extracted the data and assessed all trials to consistently evaluate their methodological quality.

A total of 34 RCTs enrolling 10,180 colorectal cancer patients were identified. The majority of the studies (74%) examined metastatic patients. 26% of the RCTs examined HRQOL as a primary endpoint. Different HRQOL measures were used to assess outcomes, with the EORTC QLQ-C30 being the most common measure used (47%). The remaining trials used different

measures, including the HADS, the RSCL and VAS. 24% of the studies had a pre-trial hypothesis on possible HRQOL changes and only 9% gave a rationale for selecting a specific HRQOL measure. HRQOL baseline and HRQOL missing data were reported in 62% and 41% of the trials respectively. 50% found some HRQOL difference between treatment arms, although sometimes this was limited to specific aspects (e.g. only few symptoms).

These studies demonstrate lack of consistent standards for incorporating HRQOL data in clinical trials in colorectal cancer. While conducting HRQOL studies are far from simple, if HRQOL RCTs are to continue to be a valuable source of information for clinical decision making for our patients, attempts to improve the quality of the conduct and reporting of our trials should continue in the key areas identified within this review.

904A POSTER

An open-label study of filgrastim in diverse nonmyeloid malignancies: phase 4 experience in community practice

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Filgrastim, a recombinant growth factor that stimulates growth and function of neutrophils, is in wide clinical use for decreasing infection in patients (pts) receiving myelosuppressive chemotherapy. Ninety-nine community oncology practices participated in a large open-label study of filgrastim. Endpoints included incidence and duration of neutropenia and percent of chemotherapy cycles given on time at planned dose. Any nonmyeloid malignancy and all standard chemotherapy regimens were allowed. Filgrastim was given per labeling (starting 24 hours after chemotherapy in all cycles, to a postnadir ANC $\geq$ 10 x 10^9/L). Blood counts were taken at least twice per week. 780 pts completed a total of 3197 cycles. Median (range) age was 58 (< 1, 91), 64% were female, and median Karnofsky score was 90. 33 tumor types were treated, the most common being breast (226 pts), lung (213 pts), non-Hodgkin's lymphoma (102 pts), ovarian (73 pts), bladder, and sarcoma (24 pts each).

	No. pt-cycles	Result
Incidence of ANC < 0.5 x 10^9/L (%)	3081	17% (16, 18)
Days of ANC < 0.5 x 10^9/L [mean (SD)]	3081	0.4 (1.1)
Cycles given on time [% (95% CL)]	3092	91% (90, 92)
Chemotherapy at full dose [% (95% CL)]	3092	90% (89, 91)
Cycles on time at full dose [% (95% CL)]	3092	85% (84, 86)
Day 14 ANC $\geq$ 2.0 x 10^9/L [% (95% CL)]	2799	93% (92, 94)

Mean number of filgrastim doses per cycle was 11.2 (SD 3.5) and was consistent across tumor types and cycles. The highest rate of initial events of grade 4 neutropenia (ANC < 0.5 x 10^9/L) was in cycle 1. Grade 4 neutropenia was observed at least once in 38% (95% CL: 35, 41) of pts, although mean duration was short (0.4 days). Risk factors for neutropenia included Karnofsky score (< 80) and young age (< 18 years); neutropenia in cycle 1 also predicted a higher rate in subsequent cycles. A high proportion of chemotherapy cycles were at full dose and on time. By day 14, 93% of pts were eligible for the next cycle based on ANC. Filgrastim facilitated planned delivery of chemotherapy with a low rate of neutropenic complications when used as labeled.

905 POSTER

Documenting symptom palliation with chemotherapy using the LCSS-Meso: Results from the randomized trial of pemetrexed plus cisplatin vs cisplatin alone in patients with malignant pleural mesothelioma

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Introduction: Malignant pleural mesothelioma (MPM) is a highly symptomatic disease with more than 90% of patients reporting three or more symptoms (any severity) at presentation. Pain and dyspnea are among the most frequent problems and a major goal of treatment is palliation. Using prospectively collected data from a 448-patient, randomized, single-blind trial, we investigated the relationship between tumor response and treatment regimen on symptom palliation.

Methods: All patients were chemonaive, and were treated with either pemetrexed (ALIMTA®) plus cisplatin (pem/cis) or cisplatin alone. Quality of life (QoL) and individual symptom scores were assessed with the LCSS-Meso, a reliable and valid instrument for patients with MPM (scores reported 0-100). Scores were transformed such that a positive change represented symptom improvement. The maximum change from baseline for both pain and dyspnea was calculated for each patient. Tumor response criteria were similar to RECIST. Patients were grouped by best overall response classified as: partial or complete response (PR/CR), stable disease (SD), or progressive disease (PD/other). The two-factor analysis of variance model included tumor response group, treatment regimen, and tumor response × treatment interaction as factors. The analysis was performed for both pain and dyspnea.

Results: The pem/cis arm had superior survival (12.1 vs 9.3 months, p=0.020), time to progression (5.7 vs 3.9 months, p=0.001) and tumor response (43% vs 17%, p<0.001). Of the 448 pts, >95% were included in the symptom-response analyses. Least square means for pain and dyspnea were as follows:

	Pain		Dyspnea	
Response group	Pem/cis	Cis	Pem/cis	Cis
PR/CR	15.3 (n=92)	8.7 (n=37)	11.9 (n=92)	8.4 (n=37)
SD	10.2 (n=77)	7.8 (n=94)	6.9 (n=77)	10.1 (n=94)
PD/other	7.0 (n=41)	-0.2 (n=87)	0.3 (n=42)	-2.1 (n=87)

The treatment regimen was significant for pain (p=0.017) with greater palliation in the pem/cis arm. For both pain and dyspnea, no statistical differences were detected between responders and SD; but scores for patients with PD were significantly different than scores for patients who responded (p<0.004) and scores for patients with SD (p<0.04). Results were similar for other LCSS-Meso scales.

Conclusions: We conclude that: 1) MPM patients who achieved tumor response or stable disease also experienced symptomatic benefit; 2) patients who were treated with pemetrexed plus cisplatin and achieved either a response or stable disease had greater symptomatic benefit than patients treated with cisplatin alone, particularly for pain; and 3) these results support the validity of LCSS-Meso for assessing subjective factors in patients with MPM. These findings support the need to monitor palliative endpoints when treating patients with highly symptomatic diseases.

906 POSTER

Nutritional counselling vs commercial supplements vs ad lib: a prospective randomised controlled trial in head-neck cancer patients undergoing radiotherapy

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Rationale: Evidence ascribing benefits to nutritional counselling with or without supplementation in cancer is as yet lacking.

Methods: In a prospective block randomised controlled trial, the effect of individualised counselling or supplements on oral intake was investigated. There were 75 head-neck cancer outpatients (pts), 60M:15F, age 60±11(36-84), stratified by cancer staging; 25 (G1) were assigned to individualised counselling based on foodstuffs, 25 (G2) to high protein liquid supplements and 25 (G3) to *ad lib* intake. Compliance was weekly monitored. Nutritional intake was assessed by a 24hr recall questionnaire at the onset, at the end and 3 months after RT; total energy requirements (ER) were=estimated basal requirements× 1.2 activity factor, protein intake was compared to reference. ANOVA stratified by staging, adjusted for symptoms, was used for comparisons.

Results: Baseline intake was similar in all groups; energy was similar to ER, protein was lower than needs, p=0.056. During RT, 92% pts experienced increased severity of odynophagia/dysphagia (p=0.005) and anorexia, p=0.01; symptoms were worse in staging III/IV, p=0.02. At the end of RT by comparison to the onset, there was an average increase of energy intake both in G1 (501 kcal/d, p=0.003) and G2 (322 kcal/d, p=0.01); G1>G2, p=0.001; protein intake increased in G1 (26g/d, p=0.007) and in G2 (35g/d, p=0.001); G1<G2, p=0.05. Energy/protein intake decreased in G3, p<0.001. At 3 months follow-up, G1 pts still complied with nutritional recommendations along with energy/protein intake improvement, whereas in G2 and G3 intake had decreased to baseline.

Conclusions: Despite baseline nutritional deficit markedly worsened by RT induced symptoms, even in advanced cancer nutritional counselling and diet supplementation did improve patients' intake. During RT, oral supplementation was a more effective protein intake restorer, whilst individualised counselling and education assured a sustained adequate diet in the medium-term.