schedule, 3 pts received XELOX (9 cycles, median 4) and 2 pts received XELIRI (7 cycles, median 3.5). Median relative dose intensity was: 98% for capecitabina and 100% for oxaliplatin, 80% for capecitabina and 92% for irinotecan during 1st XELOX/XELIRI sequence. In 19 evaluable pts for efficacy, the ORR was 47% (95% CI, 25–70%). 13 pts are not evaluable (4 adverse events; 8 on treatment and 1 lost of follow-up). The median TTP was 11.9 months (95% CI, 4.4–19.5). There were no grade 4 adverse events. Main toxicities per patient has shown in the table.
Conclusions: Sequential schedule of XELOX followed by XELIRI has shown a good safety and efficacy, including a promising low rate of grade 3 neurosensory/paresthesia toxicity in the fist-line treatment of MCRC.

704 PUBLICATION

Does radiotherapy technique influence survival in rectal cancer? A multivariate analysis

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Aim: Treatment results of postoperative chemoradiotherapy (CRT) and the effect of radiotherapy techniques on the outcome in local or advanced rectal cancer were investigated.
Patients and Methods: A total of 69 patients (39 male, 30 female) with surgically removed rectal cancer (pT3–4 pN0-any pT pN+) treated with postoperative CRT between July 1999 and December 2004 were analyzed retrospectively. Median age was 58 (24–83) years. Low anterior resection was performed in 39 patients and abdominoperineal resection in 30. The median number of removed and metastatic lymph nodes was 12 and 2 (1–49) respectively. Patients were pathologically staged as follows: IIa 39%, IIb 4.3%, IIIa 5.8%, IIIb 31.9 and IIIc 18.8%. Irradiation was given with a single daily fraction of 1.8 Gy to a total dose of 50.4 Gy. Five patients treated with the parallel opposed (AP-PA) fields and four-field box technique was used in 65 patients. Chemotherapy (CT) consisted of the combination of 5-fluorouracil and leucovorin. Thirty patients received 1 to 2 cycles of CT before concurrent CRT, while 39 has started with CRT simultaneously after surgery. The median interval between surgery and radiotherapy (RT) was 58 days and RT was completed in median 42 (30–73) days. Clinical and pathologic variables including age, sex, clinical stage, operative method, tumor differentiation, number of removed and metastatic lymph nodes, AP/PA or box treatment designs, administration of CT before RT and having late complications were analyzed using univariate and multivariate Cox models.
Results: The median follow-up was 25 (5.5–65) months. Late severe intestinal toxicity appeared in 7 patients and 5 of them had required intestinal resections, the others had occlusive crises responded to medical treatments. Local recurrence and distant metastasis were detected in 5 (%7.2) and 7 (%10.1) patients respectively.
Median progression-free and overall survivals (OAS) were 55 and 58 months. Univariate analysis showed that number of metastatic lymph nodes, AP-PA field technique, late complications and having 1 to 2 course of chemotherapy before CRT had significant impact on overall survival (OAS). In multivariate analysis, high number of metastatic lymph nodes ($p = 0.001$, HR:1.12), AP-PA field technique ($p = 0.004$, HR:8.14) and late complications ($p = 0.033$. HR: 0.21) were independent poor prognostic factors for overall survival.
Conclusion: High number of positive lymph nodes, AP-PA radiotherapy technique and late complications were independent prognostic factors for survival in patients with rectal carcinoma treated with surgery and postoperative CRT. Our results show that appropriate RT technique should be utilized for rectal cancer patients in order to improve survival.

705 PUBLICATION

Transanal excision of rectal villous adenomata is an effectine alternative to more major surgery in high risk patients

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Background: Flat adenomata are frequently unsuitable for endoscopic snare removal techniques, but those within the lower rectum may be amenable to simple transanal excision. The aim of our study was to evaluate the complication and recurrence rates in all patients who had undergone a transanal excision for rectal villous adenomata under the care of single colorectal surgeon.
Material & methods: All patients who had undergone this procedure over nine year period were identified from consultant's logbook and all casenotes were retrieved for retrospective analysis.
Results: A total of 56 trans anal excisions were performed in 35 patients. The male:female distribution was equal and the patients ranged in age from 44 to 89 years (mean age 68). Many were frail, a number having significant co-morbidity with 11 classified as ASA grade 3 or 4. All had confirmed tubulovillous adenomata with low to high grade dysplasia. The distance of the lesions were ranging 4 cm-10 cm (mean 6 cm) from anal verge. Recurrence developed in 5 patients (14%), of which 3 underwent repeat excision, 2 elderly patients having multiple repeat procedures over many years. There was no significant mortality or morbidity.
Conclusions: Transanal excision is a successful alternative to major surgical operations in relatively poor risk patients with large rectal villous adenomas, with no significant mortality and morbidity.

706 PUBLICATION

Comparision of rectal bleeding clinic with conventional out patient clinic for detection of early colorectal cancer.

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Background: To study the effectiveness of a Rectal Bleeding Clinic in detecting premalignant colonic lesions and early colorectal cancers in comparison with conventional out-patient clinics (OPD).
Materials & methods: All 2,175 consecutive patients referred to the RBC from November 1997 to Aug 2004 were assessed by detailed history, clinical examination and flexible sigmoidoscopy underwent subsequent colonoscopy. The final definitive histology of each patient was confirmed from the histology department database, which was also used to identify a control group of 92 consecutive patients with colorectal cancer diagnosed in conventional OPD.
Results: Two hundred and thirty patients (10.6%) had significant neoplastic lesions. Of these 139 had adenomatous polyps and 92 patients had invasive cancer. Of the invasive cancers, forty one (45%) patients had Duke's A lesions, as compared to 10 (10%) of the control group of patients coming through the OPD during this period, as shown in the table below.

Duke's stage	RBC	OPD
A	41 (45%)	10 (10%)
B	29 (29%)	43 (46%)
C	17 (19%)	31 (36%)
D	4 (4%)	5 (5%)
X	3 (3%)	3 (3%)
Total	*92*	*92*

Twenty patients ages 40–49 years were diagnosed as having neoplastic lesions (eleven with low grade dysplasia, one with high grade dysplasia and eight with invasive cancer).
Conclusions: A rapid access RBC enables detection of a higher proportion of potentially curable early colorectal cancers than conventional clinics, in addition to a large number of pre-malignant lesions which can be treated endoscopically with subsequent colonoscopic surveillance.

707 PUBLICATION

Capecitabine, oxaliplatin and irinotecan combination: a first line treatment for metastasic colorectal cancer, preliminary results of a phase II study

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Background: Oxaliplatin, Irinotecan and Capecitabine are active drugs in colorrectal cancer. This drugs have been found to act sinergistically, both, at "in vivo" and "in vitro" studies. The aim of this study is to determinate the safety and efficacy of this combination in metastasic colorrectal cancer (MCRC) as first-line treatment.
Methods: 34 eligible and untreated patients with MCRC were included in this trial. All patients received, Oxaliplatin 85 mg/m^2 day 1, Irinotecan 150 mg/m^2 day 1 and Capecitabine 800 mg/m^2 bid for 7 days, cycles were repeated every 14 days.
Results: From November 2004 to May 2005, 34 patients were enroled into the study with the following characteristics: male/female (64.7%/35.3%), median age 57 (32–68), performance status 91.2% I, 8.8% II, metastasic locations: 85.3% liver, 79.4 lung, 25% retroperitoneum. The median number of cycles received per patient was 6 (1–12). Response was as follows: 5.9% complete response, 73.5% partial response, 20.5% stabilization. No progressions during treatment were found.
NCI-CTC grade III/IV hematologycal toxicities presented as follows: 8.8% Anemia, 11.8% leucopenia, 32.4% neutropenia, 2.9% plaquetopenia. Non-hematologycal toxicities presented as follows: 14.7% vomiting, 14.7%

dhiarrea, 2.9% astenia. The median follow-up time was 6.7 months. Disease-free survival and overall survival data are not avaliable yet.
Conclusions: Our preliminary results suggest that Capecitabine, Oxaliplatine and Irinotecan as first-line combination treatment in MCRC is a feasible and safe schedule with high antitumoral activity. More data will be presented when follow-up time increases.

708 PUBLICATION

Total pelvic exenteration for pelvic malignancies

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Introduction: Complete resection is the most important prognostic factor in surgery for pelvic tumours. In locally advanced and recurrent pelvic malignancies radical margins are sometimes difficult to obtain, because of close relation to or growth in adjacent organs/structures. Total pelvic exenteration (TPE) is an exenterative operation for these advanced tumours and involves en bloc resection of the rectum, bladder and internal genital organs (prostate/seminal vesicels or uterus).
Methods: Between 1990 and 2003 a TPE was performed in 47 patients with pelvic cancer; 29 rectal cancer (19 primary and 10 recurrent), 12 cervical cancer (2 primary and 10 recurrent), 4 sarcoma (2 primary and 2 recurrent), 1 primary vaginal – and 1 recurrent endometrial carcinoma. Eleven patients were previously treated with radiotherapy. Two patients were treated with neo-adjuvant chemotherapy. Thirty-three patients received pre-operative radiotherapy to induce downstaging of the tumour and three patients received post-operative radiotherapy. Thirteen patients received IORT because of an incomplete or marginal complete resection.
Results: The median follow up was 25 months (range 3–145). Median operation-duration, blood loss and hospitalisation were 440 min (range 300–670), 6300 ml (range 1100–21000) and 20 days (range 12–65). Overall major and minor complication rates were respectively 34% and 57%. The hospital mortality rate was 2%.
A complete resection was possible in 72% of all patients, a microscopically incomplete resection (R1) in 19% and a macroscopically incomplete resection (R2) in 9%.
Five-year local control for primary locally advanced rectal cancer, recurrent rectal cancer and recurrent cervical cancer was respectively 86%, 51% and 67%. Overall survival after 5 year for primary locally advanced rectal cancer, recurrent rectal cancer and recurrent cervical cancer was 46%, 23% and 67%.
Conclusion: Although total pelvic exenteration is accompanied with considerable morbidity, good local control and acceptable overall survival justifies the use of this extensive surgical technique in patients with primary locally advanced and recurrent pelvic tumours. New (neo)adjuvant treatment modalities will further improve complete resection rate, local and overall survival rate.

709 PUBLICATION

Preoperative radiotherapy and oral capecitabine improve surgical results in patients with locally advanced mid-lower rectal cancer

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Background: Preoperative chemoradiation increases the chances downstaging and downsizing of locally advanced rectal cancer and facilitates sphincter-saving procedures with significant impact on disease control and quality of life.
Material: 74 patients with T_{3-4} and/or N+ (according rectal endosonography) mid and low rectal adenocarcinomas were treated with preoperative chemoradiation consisted of capecitabine (825 mg/m^2) twice daily and radiotherapy in daily dose 1.8 Gy (25 days) followed by a boost up to 50.4 Gy. The patients were operated six weeks after finishing chemoradiation. Surgical procedures included total mesorectal excision and various modifications of stapled low colorectal anastomosis or abdominoperineal excision.
Results: Downstaging was observed in 73% of patients, 18% of patients had no residual disease. 19 abdominoperineal excisions and 53 low anterior resections were performed. Two anastomotic leaks were noticed during the postoperative period. One local recurrence has been registered so far. Two patients with complete remission are being observed without operation.
Conclusion: Preoperative chemoradiation with oral capecitabine works well in downsizing and downstaging of locally advanced rectal cancer and has resulted in more sphincter preservation operations and pelvic disease control with minimal perioperative and late morbidity. The impact on long-term disease control and survival requires further follow-up.

710 PUBLICATION

Cetuximab reversal of chemotherapy resistance in patients with extensively pretreated metastatic colorectal cancer treated at Paul-Brousse hospital

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Background: Cetuximab has demonstrated activity both as single agent and combined with irinotecan in patients (pts) with colorectal cancer (CRC) refractory to irinotecan (CPT-11) and oxaliplatin expressing epidermal growth factor receptor (EGFR). This retrospective study explored the activity and tolerability of cetuximab-5-fluorouracil-leucovorin (5-FU-LV) combined with CPT11 and /or oxaliplatin (l-OHP) in pts with CRC refractory to 5-FU-LV, CPT11 and l-OHP.
Methods: 37 pts were treated with cetuximab at 400 mg/m^2 loading dose over 2 hours, then 250 mg/m^2 over 1 hour weekly. Cetuximab was given alone (1 pt) or combined with CPT11–5-FU-LV +/-l-OHP (29 pts) or l-OHP-5-FU-LV (7 pts) given as conventional (5 pts) or chronomodulated infusions (31 pts). EGFR status (0 vs 1–10 vs >10% positive cells) was determined with Dako (12 pts), Zymed (17 pts) or Ventana (8 pts). Toxicity was graded every 2–3 weeks (Common Toxicity Criteria). Response was assessed with CT scan every 2 months (RECIST criteria).
Results: 28 pts with EGFR+ and 9 pts with EGFR− CRC received treatment as 3rd line or beyond. Median age 64 y; M/F: 16/21; WHO performance status 0/1/2: 20/14/3; colon/rectum: 23/14; ⩾2 metastatic sites: 30 pts. Cetuximab was withdrawn for allergic reaction during 1st course in 5 pts. Any grade 3–4 toxicities were encountered in 47.5% of the pts. The major toxic effect was acneiform skin rash which occurred in 20 pts (grade 2: 12 pts, 32.4%; grade 3, 8 pts, 21.6%). Four pts are not assessable for response (no measurable disease: 1 pt; too early: 3 pts). Of 33 pts, treatment failed in 10 pts (30.3%), disease was stable in 12 pts (36.4%), partial responses (RECIST criteria) occurred in 9 pts (27.3%) and complete responses in 2 pts (6%). Response rate was 33.3% [95% CL: 17 to 49.7%]. Disease was controlled (response or stabilization) in 23 pts (69.7%). No obvious relation was found between: 1) EGFR status and response (EGFR 0%, 1 CR / 5 pts; EGFR 1–10%, 6 PR /14 pts; EGFR >10%, 1 CR & 3 PR /9 pts) or 2) grade of acneiform rash and response (grade 0–1, 5/11 pts; grade 2, 3/11 pts; grade 3, 3/6 pts).
Conclusions: The combination of cetuximab with the chemotherapy regimens here administered apparently increased response rate with acceptable tolerability as compared to that reported in the BOND study. This supports a supradditive effect of cetuximab which here appeared as unrelated with immunohistochemistry-assessed EGFR status or grade of acneiform reaction.

Oral presentations (Thu, 3 Nov, 8.30–10.30)
GI – GIST tumours

711 ORAL

Imatinib mesylate in advanced Gastrointestinal Stromal Tumors (GIST): survival analysis of the intergroup EORTC/ISG/AGITG randomized trial in 946 patients

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Background: From 2/2001 to 2/2002, 946 patients (pts) with a diagnosis of advanced GIST were randomized to Imatinib at two dose levels within a