is the initial report of the impact of HTN development and treatment in a population-based observational study that had no prespecified patient characteristics for study participation. Thus, the findings are more reflective of the outcomes associated with general use of BV.
Methods: Population and methods have been described previously (Kozloff, ASCO 2006; A3537). Data on HTN requiring medication and specific classes of anti-HTN medications were collected at baseline and on a quarterly basis. Blood pressure readings were not collected. HTN was defined as requirement for anti-HTN medications. "Increased HTN" was defined as any anti-HTN medication dose increase or addition.
Results: Of 1953 evaluable patients, 827 (42.3%) patients had HTN at baseline; 155 (18.7%) patients developed increased HTN over the treatment course. Frequency of increased HTN was dependent on intensity of baseline anti-HTN; the rate was lowest in patients with ⩾3 anti-HTN classes of medications at baseline. A total of 1126 patients were without HTN at baseline; 207 (18.4%) developed HTN; 48.3% of these de novo HTN patients required modification of anti-HTN medications due to increased or uncontrolled HTN. Use of specific classes of anti-HTN medications was similar for patients with or without baseline HTN. The majority of patients had only 1 modification of anti-HTN medications over the treatment course regardless of the presence of baseline HTN. There have been only 8 patients with a BV-related HTN SAE.
Conclusions: In BRiTE, a large BV treatment registry, there was no difference in the percentage of patients requiring treatment of BV-associated HTN based on the presence of HTN at baseline. These findings suggest that HTN at baseline does not increase the risk of developing increased HTN associated with BV use. Furthermore, the rate of HTN observed in BRiTE is comparable to rates seen in controlled BV trials suggesting that use of BV in the general patient population continues to be well tolerated.

3050 POSTER

A prospective analysis of the incidence of local recurrence in relation to the macroscopic and microscopic distal bowel margin in patients with rectal cancer receiving preoperative radiotherapy

A. Rutkowski[1], K. Bujko[2], E. Chmielik[3], A. Nasierowska-Guttmejer[4], M.P. Nowacki[5], R. Sopylo[5], A. Wojnar[6], L. Kepka[7]. *[1]Center of Oncology – Warsaw, Department of Colorectal Cancer Disease, Warsaw, Poland; [2]Center of Oncology – Warsaw, Department of Radiotherapy, Warsaw, Poland; [3]Cancer Center, Department of Pathology, Gliwice, Poland; [4]Center of Oncology-Warsaw, Department of Pathology, Warsaw, Poland; [5]Center of Oncology-Warsaw, Department of Colorectal Cancer Disease, Warsaw, Poland; [6]Silesian Oncological Center, Department of Pathology, Wroclaw, Poland; [7]Center of Oncology-Warsaw, Department of Radiotherapy, Warsaw, Poland*

Background: The primary end-point of our randomized trial was sphincter preservation. The secondary aim was to find out whether short distal bowel margin (⩽1 cm) is associated with a greater risk of local recurrence as compared to a longer margin.
Material and Methods: The study randomised 312 patients with cT3−4 resectable low-lying and mid rectal cancer to receive either preoperative irradiation (25 Gy in 5 fraction of 5 Gy) with total mesorectal excision (TME) within 7 days or chemoradiation (50.4 Gy in 28 fractions of 1.8 Gy, bolus 5-fluorouracil and leucovorin) and TME 4−6 weeks later. In patients after sphincter-preserving surgery pathologists prospectively measured macroscopic and microscopic distal bowel margins. Macroscopic margin was defined as the distance between distal edge of the macroscopic tumour or scar tissue (in case of clinical complete response) and resection bowel margin. Microscopic margin was defined as the distance between the most distally located cancer cells in a bowel wall or distal edge of the mucosal ulceration (in case of pathological complete response) and resection bowel margin.
Results: The sphincter preservation, macroscopic and microscopic distal bowel margin, local control, disease-free survival and overall survival did not differ in the both randomized groups. The pooled analysis of the both randomised groups showed that the cumulative incidence of local recurrence at 4 years (median follow-up) for patients with macroscopic margin ⩽1 cm (N = 42) and >1 cm (N = 121) was 11.3 and 15.8%, respectively, p = 0.48, hazard ratio (HR) 0.68, 95% confidence interval (CI) 0.23−2.01. The corresponding values for patients with microscopic margin ⩽1 cm (N = 44) and >1 cm (N = 96) were 11.1% and 18.6%, p = 0.28, HR 0.55, 95% CI 0.19−1.66.
Conclusions: For patients receiving preoperative radiotherapy the risk of local recurrence did not increase in those with macroscopic or microscopic bowel margin ⩽1 cm as compared to those with longer margin.

3051 POSTER

Phase II trial of sequential chemotherapy with capecitabine and irinotecan followed by capecitabine and oxaliplatin in elderly vulnerable patients (pts) with metastatic colorectal cancer (MCRC)

S. Cupini[1], S. Bursi[1], G. Masi[1], F. Loupakis[1], C. Barbara[1], L. Fornaro[1], G. Allegrini[1], R. Di Marsico[1], M. Andreuccetti[1], A. Falcone[2]. *[1]Az USL 6, Division of Medical Oncology, Livorno, Italy; [2]University of Pisa, Department of Oncology, Pisa, Italy*

Background: The overall survival of MCRC pts is correlated with the rate of pts who received all the 3 active cytotoxics (fluoropyrimidine, oxaliplatin and irinotecan) in the course of their disease. Elderly vulnerable pts are frequently excluded from clinical trials and are often treated suboptimally in the clinical practice. Clinical trials to validate in this setting the results obtained in the younger population are needed.
Patients and Methods: We enrolled in this phase II trial MCRC pts aged 75−85 years, or pts 70−75 years old but with ECOG PS 1 or 2, previously untreated with chemotherapy (CT) for advanced disease, with measurable and not resectable disease. To exclude frail pts, a comprehensive geriatric assessment (CGA) was performed baseline. Pts received irinotecan 180 mg/sqm day (d) 1 plus capecitabine 1500 mg/sqm/d d1−14 repeated every 3 weeks (ELD-XELIRI) up to 9 cycles. After progression or treatment interruption because of toxicity, pts received oxaliplatin 100 mg/sqm d1 plus capecitabine 1500 mg/sqm/d d1−14 repeated every 3 weeks (ELD-XELOX) up to 9 cycles. After a planned interim analysis, irinotecan dose was reduced to 150 mg/sqm because of an excessive incidence of diarrhea.
Results: Up today 30 pts have been enrolled and 24 pts (80%) have received both regimens. Baseline patients' characteristics are: median age 76 years (70−82), ECOG PS 1 83%, multiple sites of disease 53%, previous adjuvant CT 7%. A median of 9 cycles of first-line ELD-XELIRI per pts have been administered. Grade 3−4 observed toxicities were: diarrhea 37%, vomiting 3% and neutropenia 7%. Objective responses and stable disease were respectively 27% and 50% and median PFS was 7.3 months (mos). A median of 5 cycles of second-line ELD-XELOX per pts have been administered and the only grade 3−4 toxicity observed was diarrhea (8%). Objective responses and stable disease were respectively 10% and 52% and median PFS was 4.9 mos. After a median follow up of 31.0 mos the median time to second progression (primary objective) was 11.8 mos and the median survival was 19.3 mos.
Conclusions: These data indicate that the CGA is a useful instrument to evaluate elderly pts and to select them for treatment. The sequential treatment with ELD-XELIRI followed by ELD-XELOX is feasible in elderly vulnerable MCRC pts and it produces results comparable to those obtained in the younger population. (Partially supported by Fondazione ARCO)

3052 POSTER

Impact of diabetes mellitus on the development and outcomes of colorectal cancer

P. Gibbs[1], N. Murigu[2], J. Johns[2], S. Kosmider[1]. *[1]Royal Melbourne Hospital, Medical Oncology, Melbourne Victoria, Australia; [2]Royal Melbourne Hospital, Molecular Medicine Informatics Model (MMIM), Melbourne Victoria, Australia*

Background: Diabetes mellitus (DM) is reported to be a risk factor for colorectal cancer (CRC), and to adversely influence the tumour specific outcomes. Previous studies however have had limited detail regarding CRC pathology and staging, and the potential impact of the frequently associated obesity.
Methods: Via the MMIM comprehensive CRC database, patients with CRC were identified and the impact of DM was examined.
Results: 1116 patients with CRC were identified, 327 (29%) of whom were diabetic. Diabetics patients were significantly older at diagnosis (median age 67 vs 70 years, p = 0.002), more likely to be male (61% vs 54%, p = 0.004) and more overweight than those without diabetes (median Body Mass Index 28 vs 26, p < 0.001). Analysis of pathology revealed more poorly differentiated tumours in the diabetic patients (34% vs 19%, p < 0.001), but no difference in frequency of mucinous tumours or lymphovascular invasion. The observed difference in tumour differentiation was independent of BMI.
There was no statistically significant difference in stage at presentation, or tumour location between the two groups. Examination of survival data revealed a significantly lower 5 year overall survival rate for diabetics. Stage specific survival for diabetics with stage I and III CRC was significantly lower than non-diabetics. This difference was not significant in stage II and IV disease.
Conclusion: Our data implies diabetes is a strong risk factor for the development of CRC, as the incidence of diabetes in our patient population would be expected to be less than 10%. We report the novel finding of significant differences in pathology between diabetic and non-diabetic patients.

Our data suggests that the poor outcomes reported for diabetic patients in other studies are potentially explained by multiple factors that bias for poor tumour related outcome and overall survival. The inferior survival for diabetics with stage I CRC is likely due to death from non-cancer related causes, possibly cardiovascular complications. Follow up data examining disease free survival for stage III CRC for each group will determine if inferior outcomes in diabetics is due to increased cancer relapses, perhaps related to less well differentiated tumours.

3053 POSTER

Phase II study of combination with irinotecan and S-1 (IRIS) for inoperable recurrent advanced colorectal cancer (HGCSG0302). Safety analysis

S. Yuki[1], Y. Komatsu[1], N. Machida[1], M. Ozasa[1], K. Nishi[2], T. Miyagishima[2], T. Kato[2], M. Nakamura[2], M. Asaka[1], Y. Sakata[3]. *[1]Hokkaido University Graduate School of Medicine, Gastroenterology, Sapporo, Japan; [2]Hokkaido Gastrointestinal Cancer Study Group, Gastroenterology, Sapporo, Japan; [3]Misawa city hospital, Medical Oncology, Misawa, Japan*

Background: We planned to conduct a phase II study of combination with irinotecan and S-1, a new oral anticancer drug of the fluorinated pyrimidine type. We reported the interim reports of this study in colorectal cancer patients at ASCO 2006.
Methods: The antitumor effect was the primary endpoint, while the safety, progression-free survival time, and median survival time were the secondary endpoints. The subjects were untreated patients with inoperable advanced colorectal cancer aged 20−75 years. Irinotecan was administered at a dose of 100 mg/m^2 (on days 1 and 15) as an intravenous infusion over 90 minutes, and oral S-1 (40 mg/m^2) was administered after breakfast and dinner and then withdrawn for 2 weeks.
Results: Forty patients were enrolled in the present study. There were 23 men and 17 women. The median age was 62 years (range: 34 to 74 years). Two patients showed grade 4 neutropenia, but the next course could be given safely after dose reduction. Three patients had grade 3 diarrhea, but therapy could be continued with addition of an antidiarrhea drug. No other serious adverse reactions occurred (either hematological or non-hematological), and all patients could receive therapy safely on an outpatient basis. Forty pts. are evaluable for efficacy: RR was 52.5% (CR 1, PR 20, SD 17, PD 2, 95% CI, 37−68%) and Disease Control Rate (CR+PR+SD) was seen in 96.0% of pts. PFS of this regimen is 311 days. MST is not reached.
Conclusions: IRIS therapy achieved a high response rate and could be given safely. These findings suggest that the therapy has potential as first-line treatment for inoperable advanced recurrent colorectal cancer. It seems that IRIS is a good treatment equal to FOLFIRI. Non-inferiority randomized Phase III trial of IRIS vs. mFOLFOX6 (IFOX study) was planned, and it has been already started now. The latest data will be reported at the meeting.

3054 POSTER

Comparison of paired patient primary and liver metastatic colorectal cancer (CRC) tissues for epidermal growth factor receptor (EGFR) protein expression and the presence of mutations in the EGFR tyrosine kinase domain

J.A. Maroun[1], D.J. Jonker[1], H.C. Birnboim[1], T. Moyana[2], D. Wang[2], D. Samson[1], I. Gorn[1], I. Teo[2], G. Chiritescu[1], H. Marginean[1]. *[1]The Ottawa Hospital Regional Cancer Centre, Medical Oncology, Ottawa, Canada; [2]The Ottawa Hospital, Anatomical Pathology, Ottawa, Canada*

Background: Previous studies indicate that drugs that target the EGFR signaling pathways can induce objective responses, prolong time to progression and improve survival for CRC patients with EGFR expression in their primary tumour. However EGFR expression in the primary tumour may not predict response in the metastatic location, and little information is available about the correlation of EGFR expression between the primary tumour and the metastatic site. In other tumour sites, the presence of EGFR mutations was associated with efficacy in a subset of patients.
Objectives: The goal of this study is to correlate EGFR expression (using immunohistochemistry, IHC) between primary and liver metastatic sites of the tumour and to assess the mutational status in the EGFR kinase domain. We anticipate that high levels of EGFR will be expressed in metastatic lesions when compared to the primary tumor.
Methods: This is a retrospective study of all patients at TOHRCC who underwent surgical resection for CRC between 1999 and 2005, for whom paired paraffin-embedded tissue blocks of primary tumour and resected liver metastases were available. Seventy-four paired samples were identified. EGFR immunostaining was performed using the DakoCytomation EGFR pharmDx kit (DAKO) following manufacturer guidelines at the Department of Pathology, Faculty of Medicine, University of Ottawa. Two pathologists independently evaluated EGFR staining. To evaluate EGFR mutations, DNA was extracted and PCR was performed targeting exons 18, 19 and 21 encompassing most of the tyrosine kinase domain. PCR products were sequenced bi-directionally at the Sequencing Facility of the Ottawa Health Research Institute.
Results: EGFR staining and kinase domain sequencing has been completed on 25 paired samples. Analyses are ongoing and the study will be completed by the end of May 2007.
Conclusions: Final results will be presented at the meeting, and correlation between EGFR expression in primary tumour and metastasis will be evaluated.
Support: Funding provided by Bristol-Myers-Squibb and the Ottawa Regional Cancer Foundation

3055 POSTER

Cetuximab plus irinotecan in patients (pts) with metastatic colorectal cancer (mCRC) progressing on or after prior irinotecan therapy: final results of the LABEL study

C. de Cerqueira Mathias[1], F. Perazzo[2], S. Simon[3], L. Fein[4], J. Hidalgo[5], A.M. Murad[6], G. Lerzo[7], R. Esser[8], S. Scheid[9], A.C. Buzaid[10]. *[1]Nucleo de Oncologia da Bahia, Oncology Department, Salvador, Brazil; [2]CEMIC – Suc.Saavedra, Oncology Department, Buenos Aires, Argentina; [3]Hospital Israelita Albert Einstein, Oncology Department, São Paulo, Brazil; [4]Centro Oncologico Rosario, Oncology Department, Santa Fe, Argentina; [5]COIR – Centro Oncologico de Integracion Regional, Oncology Department, Mendoza, Argentina; [6]Hospital Vera Cruz, Oncology Department, Belo Horizonte, Brazil; [7]CODE – Clinica de Oncologia de Excelencia, Oncology Department, Buenos Aires, Argentina; [8]Merck KGaA, R& D Global Medical Affairs Oncology, Darmstadt, Germany; [9]Merck KGaA, Biostatistics and Data Sciences, Darmstadt, Germany; [10]Hospital Sirio-Libanes, Oncology Department, São Paulo, Brazil*

Background: Cetuximab (Erbitux®), an IgG1 monoclonal antibody directed against the epidermal growth factor receptor (EGFR), is active in combination with irinotecan in pts with mCRC progressing during or after prior irinotecan therapy. The European MABEL study investigated cetuximab in combination with irinotecan in 1147 heavily pre-treated mCRC pts, and found a 12-week progression-free survival (PFS) rate of 61%, median overall survival (OS) of 9.2 months and a predictable and acceptable safety profile.
Methods: This open, single-arm, phase II, 14 center study investigated this combination in pts with EGFR-expressing mCRC progressing on or within 3 months of at least 6 weeks (wks) of irinotecan-based chemotherapy. The primary objective was to assess the best overall confirmed response rate (RR). Secondary objectives included duration of response (DOR), progression-free survival (PFS), 6-weekly PFS rates, overall survival (OS), 3-monthly survival rates, and safety. Pts received cetuximab (initial dose 400 mg/m^2, then 250 mg/m^2 wkly), plus irinotecan at the same dose and schedule as pre-study (100 or 125 mg/m^2 wkly for 4/6 weeks; 100 or 125 mg/m^2 wkly for 2/3 wks; 180 or 210 mg/m^2 every 2 wks; 300 or 350 mg/m^2 every 3 wks).

Efficacy results

	All ITT patients (n = 79)
Overall confirmed RR, % [95% CI]	26.6 [17.3, 37.7]
Median DOR, wks [95% CI]	23.9 [17.1, 30.0]
Median PFS time, wks [95% CI]	17.4 [11.7, 18.9]
PFS rate, % [95% CI]	
6 wks	78 [69, 87]
12 wks	57 [46, 68]
18 wks	42 [31, 53]
24 wks	27 [17, 37]
Median OS, months [95% CI]	9.2 [7.9, 10.8]
Survival rate, % [95% CI]	
3 months	88 [81, 96]
6 months	65 [55, 76]
9 months	54 [43, 65]

Preliminary results: 71% (109/153, 2 pts missing) pts screened and in the database were EGFR-expressing. 79 pts were treated on-study: 40 (51%) male; median age 59 years [range, 27−82]; 70 (89%) with KPS $\geqslant$ 90. 19 (24%) pts had received $\geqslant$3 prior treatment regimens. 66 (84%) pts progressed within 30 days of their last course of pre-study irinotecan. Efficacy results are shown below. The most common grade 3/4 adverse