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

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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an intravenous infusion over 90 minutes, and oral S-1 (40 mg/m^2) was administered after breakfast and dinner and then withdrawn for 2 weeks.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

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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

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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