line CapIri and 2nd line CapOx (Arm B, combination). The dose of Cap was 1250 mg/m^2 (mono) or 1000 mg/m^2 (combination) b.i.d. day 1−14, Iri 350 mg/m^2 (mono) or 250 mg/m^2 (combination), and Ox 130 mg/m^2. All cycles were q 3 weeks with Iri/Ox given i.v. on day 1. Response was assessed every 3 cycles. Primary endpoint was OS. The study was designed to detect a 20% reduction in the hazard of death (HR = 0.80) for an increase in median OS from 14 to 17.5 months (alpha=0.05, 2-tailed test).
Results: 820 pts were randomized between Jan 2003 and Dec 2004 in 74 Dutch hospitals. Of 803 eligible pts, 795 received $\geqslant$1 cycle. Median age was 63 (27−84) yrs, median WHO PS 0 (0−2), median follow-up 32 m. Pts in arm A: 397 (1st line), 246 (2nd line), 142 (3rd line); arm B: 398 (1st line), 211 (2nd line). Median OS in arm A was 16.2 m (95% CI 14.2−18.0) and in arm B 18.0 m (15.3−19.4), logrank p = 0.19. Overall toxicity over all lines did not differ significantly except for grade 3 hand–foot syndrome (HFS) (13% in A vs 6.5% in B, p = 0.004), and incidence of cholinergic syndrome (18% in A vs 24% in B, p = 0.03). Death was probably related to treatment in 11 pts (neutropenic sepsis and/or diarrhea, 8 arm A, 3 arm B). In 1st line significant differences in grade 3−4 toxicity in arm A vs arm B were diarrhea (11% vs 26%, p < 0.0001), febrile neutropenia (1% vs 7%, p < 0.0001), HFS (12% vs 6%, p = 0.002), incidence of cholinergic syndrome (p < 0.0001), nausea (4% vs 8%, p = 0.004) and vomiting (3% vs 9% p = 0.0002). All-cause 60-day mortality was 3.0% (n = 12) in arm A and 4.5% (n = 18) in arm B.
Conclusions: Combination therapy does not significantly improve OS compared with sequential therapy. Both treatment strategies are valid options for pts with ACC. Updated results will be presented at the meeting, including data on progression free survival and response rate.

Poster presentations (Mon, 24 Sep, 09:00−12:00)
Gastrointestinal malignancies – colorectal cancer

3016 POSTER

Trends in chemotherapy (CT) utilization for colorectal cancer: A provincial population-based analysis

D. Renouf, H. Kennecke, S. Gill. *BC Cancer Agency, Medical Oncology, Vancouver BC, Canada*

Background: Significant advances have been made in the treatment of colorectal cancer in both the adjuvant and metastatic setting. The purpose of this study is to examine chemotherapy (CT) prescribing patterns for adjuvant therapy of colon cancer and metastatic colorectal cancer over the last 15 years in British Columbia, Canada.
Methods: All patients (pts) with stage 2 or 3 colon cancer, or stage 4 colorectal cancer at presentation referred to the BC Cancer Agency during a one year period for three time cohorts: 1990, 2000 and 2004, were reviewed. A pt was considered to be treated with CT if they received a cycle of CT within 6 months of referral.
Results: A total of 1421 patients were included: stage 2/3 n = 915, stage 4 n = 506. Chemotherapy utilization increased significantly from 1990 to 2004 for adjuvant CT [1990: 49 (29%), 2000: 129 (45%), 2004: 235 (52%), p < 0.001] and for palliative CT [1990: 41(35%), 2000: 100 (51%), 2004 120 (63%), p < 0.001]. The proportion of pts with stage 2 disease treated with adjuvant CT increased dramatically [1990: 3(4%), 2000: 38 (26%), 2004: 50 (30%), p < 0.001]. CT utilization was directly associated with later time cohort and younger age of presentation. The use of palliative CT was significantly associated with male gender (p = 0.025). This gender bias was not observed in the adjuvant setting. Among pts >70y, only 25% (99/394) received adjuvant CT [1990: 5(8%), 2000:38 (28%), 2004: 57 (28%)] and 31% (50/162) received palliative CT [1990:4 (15%), 2000:17 (24%), 2004:30 (45%)].
Conclusions: In this population-based cohort, adjuvant and palliative CT utilization has increased since 1990 however there is room for improvement. Despite the lack of conclusive evidence, the use adjuvant CT for stage II disease has increased significantly. Female pts appear less likely to receive palliative CT. Despite evidence that the elderly can accrue similar proportional benefits, the majority of referred pts >70y still do not receive adjuvant or palliative CT. Such discrepancies in CT utilization require further investigation.

3017 POSTER

Cetuximab dose-escalation in patients (pts) with metastatic colorectal cancer (mCRC) with no or slight skin reactions on standard treatment: pharmacokinetic (PK), pharmacodynamic (PD) and efficacy data from the EVEREST study

Y. Humblet[1], M. Peeters[2], H. Gelderblom[3], J.B. Vermorken[4], F. Viret[5], B. Glimelius[6], F. Ciardiello[7], E. Gallerani[8], O. Kisker[9], E. Van Cutsem[10]. *[1]University St-Luc, Medical Oncology, Brussels, Belgium; [2]University Hospital Gent, Medical Oncology, Gent, Belgium; [3]University Medical Center, Oncology, Leiden, The Netherlands; [4]University Hospital Antwerp, Department of Medical Oncology, Antwerp, Belgium; [5]Institut Paoli Calmettes, Oncology, Marseille, France; [6]Akademiska University Hospital, Oncology, Uppsala, Sweden; [7]Second University of Naples, Dipartimento Medico-Chirurgico di Internistica Clinica e Sperimentale, Naples, Italy; [8]Institute of Oncology of Southern Switzerland, Oncolgy, Bellinzona, Switzerland; [9]Merck KGaA, R& D Medical Sciences Oncology, Darmstadt, Germany; [10]University Hospital Gasthuisberg, Department of Gastroenterology, Leuven, Belgium*

Background: Response to cetuximab treatment appears to correlate with the intensity of the associated skin reaction. This phase I/II randomized study investigated cetuximab dose-escalation in pts with EGFR-expressing mCRC failing prior irinotecan-containing therapy.
Methods: The primary objective was to investigate the effects of dose-escalation on EGFR and downstream signaling in skin and tumor biopsies compared to standard cetuximab regimen. Secondary objectives included PK, efficacy, safety, tolerability, tumor and plasma biomarker analysis in relation to treatment, side effects and response. Pts received cetuximab (400 mg/m^2 initial dose, then 250 mg/m^2/week [w]) with irinotecan (180 mg/m^2 q2w) until randomization at day 22. Pts were randomized if they had not experienced > Grade (Gr) 1 skin reaction or any other >Gr2 cetuximab-related AE and were tolerant to irinotecan. Randomization was to Arm A (cetuximab standard dose, 250 mg/m^2/w) or Arm B (cetuximab dose increased by 50 mg/m^2 q2w, until >Gr2 toxicity, tumor response or dose=500 mg/m^2/w). Pts not randomized (Arm C) continued on cetuximab 250 mg/m^2/w. All pts continued to receive irinotecan.
Results: 284 pts were screened, 221 (78%) EGFR-expressing, 166 enrolled: 45 randomized to Arm A; 44 to Arm B; 77 non-randomized to Arm C. 106 pts (64%) were male, median age 60 years [25−79], and median KPS 90 [70–100]. In Arm B, 24 pts reached the maximum cetuximab dose. Response rate (RR) in Arm B was 30% vs 16% in Arm A (22% in Arm C). Progression-free survival in Arm B was 4.8 months vs 3.9 months in Arm A (3.9 months in Arm C). Gr3/4 skin reactions occurred in 11% of pts in Arm B, 0% in Arm A (14% in Arm C). Dose-related increases in C_{max} and AUC were observed. $T_{1/2}$ values were dose-independent. IHC analysis in skin biopsies showed no significant association of baseline levels or on-treatment changes of candidate EGFR-signalling markers with dose-escalation or response, whereas in tumor some markers show a trend for association with response. Gene candidate expression in tumor (microarray analysis) and some plasma proteins (Luminex proteomics) appear to be associated with response.
Conclusions: Pts with no or slight skin reactions on standard dose cetuximab may demonstrate improved RRs and PFS with dose-escalation up to 500 mg/m^2/w. Overall cetuximab PK behavior is in good agreement with previous experience. Treatment was generally well tolerated. Detailed PD data will be presented at the meeting.

3018 POSTER

Pharmacogenetic analysis of toxicity after 5-fluorouracil (5FU) or 5FU/Oxaliplatin therapy for metastatic colorectal cancer: Preliminary results in FFCD 2000−05 trial

V. Boige[1], M. Castaing[2], M.A. Loriot[3], M. Barrois[4], I. Miran[4], C. Mulot[3], J.P. Pignon[2], M. Ducreux[1], P. Laurent-Puig[3]. *[1]Institut Gustave Roussy, Medicine, Villejuif, France; [2]Institut Gustave Roussy, Biostatistics, Villejuif, France; [3]INSERM, U775, Paris, France; [4]Institut Gustave Roussy, Oncogenetics, Villejuif, France*

Background: The FFCD 2000−05 randomized trial compared simplified LV5FU2 followed by FOLFOX6 (arm 1) to FOLFOX6 followed by FOLFIRI (arm 2) in the treatment of metastatic colorectal cancer. The aim was predicting the toxicity profile of oxaliplatin after the first line treatment using pharmacogenetic data.
Materials and Methods: Patients (pts) with available blood samples were compared to the other pts for clinical prognostic factors (chi2 test). A logistic model was computed to test the association between polymorphisms and toxicity in each arm. An interaction test was used to assess a differential effect according to treatment (predictive effect), in order to identify a predictive effect of oxaliplatin. Grade 3−4 hematological and non-hematological