IrCs was not however confirmed: ITT analysis showed 179/335 (53.4%) pts progression-free at 12 wks with Ir, 159/337 (47.2%) with IrCs, Δ −6.3%, with the 95% CI crossing the prespecified efficacy boundary (−13.8%, +1.3%). OS was not impaired (HR 1.07 [95% CI 0.90, 1.28]).
Conclusions: IrCs was associated with less diarrhoea as assessed by lopermide use, but severe diarrhoea was uncommon in both arms. However, we failed to prove non-inferiority of IrCs compared with Ir, so cannot recommend it as a standard treatment option for aCRC based on the PICCOLO trial data.
Sponsor − University of Leeds. Status − Closed to recruitment.

6098 POSTER

CRAFT Trial-Result From Multicenter Phase II Study of Modified FOLFOX7 (Combination Chemotherapy of Infusional 5-FU/l-Leucovorin and Intermittent Oxaliplatin) With Bevacizumab in the First-line Therapy of Colorectal Cancer

K. Ishibashi[1], K. Koda[2], M. Oshiro[3], H. Matsuoka[4], H. Baba[5], H. Ishida[1], R. Katoh[3], K. Maeda[4], C. Hamada[6], J. Sakamoto[7]. [1]*Department of Digestive Tract and General Surgery, Saitama Medical Center, Saitama Medical University, Saitama, Japan;* [2]*Department of Surgery, Teikyo University Chiba Medical Center, Chiba, Japan;* [3]*Department of Surgery, Toho University Sakura Medical Center, Chiba, Japan;* [4]*Department of Gastroenterological Surgery, Fujita Health University Hospital, Aichi, Japan;* [5]*Department of Gastroenterological Surgery, Kumamoto University Graduate School of Medical Science, Kumamoto, Japan;* [6]*Tokyo University of Science, Faculty of Engineering, Tokyo, Japan;* [7]*Nagoya University Graduate School of Medicine Health and Community Medicine, Program in Health and Community Medicine, Aichi, Japan*

Background: A combination of LV+FU with oxaliplatin (FOLFOX) has been established as a standard first-line therapy for metastatic colorectal cancer (mCRC).
Therefore, prior clinical trial showed that additional bevacizumab (monoclonal antibody for vascular endothelial growth factor) to FOLFOX improved survival in patients(pts) with mCRC (NO16966 study, Saltz et al JCO2008). OPTIMOX1 study suggested that stop and go strategy for oxaliplatin reduced peripheral sensory neuropathy. However OPTIMOX study was not included Bevacizumab. Thus we conducted to confirm stop and go strategy of Bevacizumab containing FOLFOX in this trial.
Materials and Methods: Eligibility criteria included ECOG PS: 0−1, No Peripheral neuropathy (<Grade 1). Patients received mFOLFOX7 (oxaliplatin 85 mg/m^2, LV200 mg/m^2, 5FU 2400 mg/m^2 + bevacizumab 5 mg/kg q2 weeks for 8 cycles, maintenance without oxaliplatin for 8 cycles, and reintroduction mFOLFOX7 + bevacizumab for 8 cycles until progression. Primary endpoint was Progression Free Survival (PFS).
Results: Between March 2009 and June 2010, 52pts were enrolled. Baseline characteristics were median age of 64 years (range, 36−74); PS 0/1 (43/9 pts);male/female(32/20 pts), colon/rectum (25/27pts) and metastatic lesion liver/lung/lymph nodes (34/21/12 pts). A total of 48 pts were evaluated as Par Protocol Set population. 32pts moved from initial FOLFOX7 to maintenance mLV5FU2. 25pts moved to mFOLFOX7 reintroduction. Median PFS was 12.3months (95% CI, 8.6–18.2) and Median TTF was 9.9 months (95% CI, 5.3–11.4). Best overall response rate was 45%. Median mLV5FU2 courses were 7.2 cycles (range 2−8). Oxaliplatin reintroduction rate was 52%. The causes of reintroduction failure were disease progression (4 pts), successfully-liver resection (1pt), withdrawal consent (1pt), peripheral sensory neuropathy Grade 2 (1pt). Main grade 3/4 toxicity were: neutropenia (3pts), peripheral neuropathy (2pts), hypertension (2pts).
Conclusions: This study met its primary endpoint PFS. It was longer than NO16966. mFOLFOX7 without FU bolus and intermittent oxaliplatin indicated to reduce incidence of severe neutropenia and peripheral sensory neuropathy. The results suggested that our treatment strategy was well tolerate and effective for first line therapy in mCRC, and maintenance duration for 8 cycles, was reasonable.

6099 POSTER

The Value of Thymidine Kinase 1 (TK1) and Thymidine Phosphorylase (TP) Expression as Predictive Factors With the Treatment Efficacy of TAS-102, a Novel Antitumour Agent, in Patients (pts) With Metastatic Colorectal Cancer (mCRC)

Y. Komatsu[1], T. Yoshino[2], N. Mizunuma[3], K. Yamazaki[4], T. Nishina[5], H. Baba[6], A. Tsuji[7], K. Yamaguchi[8], K. Muro[9], A. Ohtsu[2]. [1]*Hokkaido University Hospital, Cancer Center, Hokkaido, Japan;* [2]*National Cancer Center Hospital East, Department of Gastroenterology & GI Oncology, Chiba, Japan;* [3]*The Cancer Institute Hospital of JFCR, Division of Chemotherapy Gastrointestinal Oncology, Tokyo, Japan;* [4]*Shizuoka Cancer Center, Division of Gastrointestinal Oncology, Shizuoka, Japan;* [5]*National Hospital Organization Shikoku Cancer Center, Department of Gastroenterology, Ehime, Japan;* [6]*Kumamoto University Hospital, Gastroenterological Surgery, Kumamoto, Japan;* [7]*Kochi Health Sciences Center, Department of Medical Oncology, Kochi, Japan;* [8]*Saitama Cancer Center, Department of Gastroenterology, Saitama, Japan;* [9]*Aichi Cancer Center Hospital, Department of Clinical Oncology, Aichi, Japan*

Background: TAS-102 is a novel oral nucleoside antitumour agent, consisting of trifluorothymidine (FTD) and thymidine phosphorylase inhibitor which prevents degradation of FTD. We will report promising results at the congress that TAS-102 (A) significantly improved overall survival (OS) compared with placebo (P) (A, n = 112; P, n = 57; median OS, 9.0 vs. 6.6 months; HR, 0.56; p = 0.001). FTD has 2 mechanisms of action: it inhibits thymidylate synthase (TS) and is incorporated into DNA molecule after phosphorylation by TK1, leading to antitumour effects that differ from TS inhibitors such as fluoropyrimidine. Therefore, TK1 and TP seem to play key roles in eliciting the potent antitumour effects of TAS-102 in cancer pts. In this clinical study we have investigated whether TK1 and TP expression levels could be useful predictive factors.
Material and Methods: Patients with mCRC who had refractory or intolerable to standard chemotherapy regimens, including fluoropyrimidine, irinotecan and oxaliplatin; had ECOG PS of 0 to 2; and had adequate organ functions were randomly assigned to TAS-102 and placebo, in a ratio of 2:1. TAS-102 or placebo was orally administered twice daily at a dose of 70 mg/m^2/day from d 1 to 5 and from d 8 to 12 every 4 weeks. The H-scores for the cytoplasmic expression of TK1 and TP were blindly scored from immunohistochemical staining. The study primary endpoint was OS, and the correlation between TK1, TP expression and efficacy was analyzed.
Results: The expression data of TK1 and TP before treatment were available for 150 and 149 of pts treated, respectively. The median H-score for TK1 expression was 115.00 vs. 115.00 (mean; A/P, 116.06/113.53) and 115.00 of two pooled groups, and the median H-score for TP expression was 12.50 vs. 15.00 (mean; A/P, 21.58/27.35). Table 1 shows multivariate analysis by Cox proportional hazard model, which included interactions between treatment and TK1 (>115 vs. ⩽115), TP (>15 vs. ⩽15) categorized according to median pooled groups.
Conclusions: TAS-102 treatment significantly improved OS in pts with mCRC. TK1 and TP expression levels were not correlated with OS in pts treated TAS-102. Additional analyses will be reported at the congress.

Table 1

Variable	OS (N = 149)		
	HR	95% CI	*p*
Treatment (A/P)	0.61	0.41 to 0.91	0.015
PS (1 or 2/0)	1.58	1.07 to 2.33	0.022
TP (>15/⩽15)	1.17	0.79 to 1.74	0.433
TK1 (>115/⩽115)	1.20	0.81 to 1.78	0.367
Treatment × TP	0.89	0.60 to 1.32	0.566
Treatment × TK1	0.90	0.61 to 1.34	0.610

6100 POSTER

Prolonged Survival of Patients With Metastatic Colorectal Cancer Who Underwent First-line Oxaliplatin Based Chemotherapy With the Introduction of Molecular Targeting Agents and Curative Surgery

K. Shitara[1], K. Matsuo[2], C. Kondo[1], D. Takahari[1], T. Ura[1], K. Muro[1]. [1]*Aichi Cancer Center Hospital, Department of Clinical Oncology, Nagoya, Japan;* [2]*Aichi Cancer Center Research Institute, Division of Epidemiology and Prevention, Nagoya, Japan*

Background: Recently, two types of molecular targeting agents were introduced for treatment of metastatic colorectal cancer (MCRC). However, it remains controversial whether these agents are associated with improved overall survival (OS) in oxaliplatin based chemotherapy.

Methods: We retrospectively analyzed 331 patients with MCRC who underwent first-line oxaliplatin based chemotherapy. Treatment outcome was compared patients who initiated chemotherapy during April 2005 and March 2007 (cohort A; n = 157) and that of patients during April 2007 and March 2009 (cohort B; n = 174). To evaluate the impact of exposure to each agent in any lines of chemotherapy, we applied time-varying covariates analysis to avoid possible lead-time bias.
Results: Median overall survival (OS) of cohort A and cohort B was 21.3 and 28.6 months, respectively, with significantly better OS in cohort B (HR 0.66, 95% CI 0.50–0.87, P = 0.003). Exposure to bevacizumab (25% vs. 76%), anti-EGFR (18% vs. 33%) or curative surgery after chemotherapy (4% vs. 10%) was significantly higher in cohort B. According to a multivariate Cox model with exposure to each agent class as a time-varying covariate, the hazard ratios (HR) of death were 0.31 (95% CI, 0.18–0.46; p < 0.001) for irinotecan, 0.71 (95% CI, 0.51–0.96; p = 0.03) for bevacizumab, 0.62 (95% CI, 0.40–0.89; p = 0.01) for anti-EGFR, 0.22 (95% CI, 0.06–0.57; p = 0.004) for surgery.
Conclusions: Increased exposure to molecular targeting agents or curative surgery after chemotherapy appears to contribute to improvement of OS in recent patients with MCRC who underwent oxaliplatin based chemotherapy.

6101 POSTER

Promising Results After Radionuclide Therapy With 177Lu-DOTA-octreotate in Patients With Disseminated Neuroendocrine Hindgut Tumours

U. Garske[1], M. Sandström[2], S. Johansson[3], P. Hellman[4], A. Sundin[5], B. Eriksson[6], D. Granberg[6]. *[1]University Hospital Uppsala, Nuclear Medicine Department of Radiology Oncology and Radiation Science Department of Medical Sciences, Uppsala, Sweden; [2]University Hospital Uppsala, Medical Physics Department of Radiology Oncology and Radiation Science, Uppsala, Sweden; [3]University Hospital Uppsala, Nuclear Medicine and Oncology Department of Radioloy Oncology and Radiation Science, Uppsala, Sweden; [4]University Hospital Uppsala, Surgery Department of Surgical Sciences, Uppsala, Sweden; [5]Karolinska Institute, Molecular Medicine and Surgery, Stockholm, Sweden; [6]University Hospital Uppsala, Endocrine Oncology Department of Medical Sciences, Uppsala, Sweden*

Background: Peptide receptor radiotherapy was introduced as a therapeutic option for neuroendocrine tumours more than a decade ago. Hindgut carcinoids have historically had only limited treatment options when metastasized. This report focuses on the outcome of this patient group after therapy with 177Lu-DOTA-octreotate.
Material and Methods: Since December 2005, 16 patients (8 M/8 F) with hindgut carcinoids have received 2−8 courses of 7.4 GBq 177Lu-DOTA-octreotate until a maximum of 23 Gy absorbed dose to the kidneys as dose limiting organs. Median age was 53years (25−75). All patients were in TNM stage IV. Ki-67 was available for 15 patients, one patient <2% (G1), 13 patients ⩽20% (G2), one patient =30% (G3). Eight out of 14 patients with liver metastases showed an involvement of more than 50% of the liver volume. Mean time from primary diagnosis to start of 177Lu-DOTA-octreotate was 39 months (2−99 months). Twelve patients had undergone resection of the primary tumour at diagnosis and one had received external radiotherapy. Six patients had been objected to chemotherapy and had progressed or suffered from intolerable side effects, eight received 177Lu-DOTA-octreotate as first line systemic treatment. Radiological evaluation was performed according to RECIST criteria.
Results: From time of diagnosis, mean-follow-up was 70 months, median 57 (range 14–139 m). Mean follow-up after start of therapy was 33.4 months, median 39 (range 11−63m). Two patients died 14 and 48 months after start of therapy, corresponding to 48/67 months after diagnosis. One patient was lost to follow-up 11 months after start of treatment, 13 are alive. Best response this far: 0% CR, PR 9 patients (56%), SD 7 patients (44%). 0% PD. Decrease of tumour burden was observed up to 57 months after start of therapy. Four patients could undergo subsequent tumour reductive surgery. Six patients progressed after initial response. Side effects: 12/16 patients showed transient thrombocytopenia, 10 grade 1&2, one grade 3, one grade 4; 9/16 showed transient neutropenia (7 grade 2, 2 grade 3, none grade 4); slightly elevated S-creatinine occurred in 4/16 patients; all grade 1.
Conclusion: Patients with advanced hindgut tumours demonstrate a high response rate and mild side effects on radionuclide therapy. 177Lu-DOTA-octreotate treatment should be considered as first line in this patient category.

6102 POSTER

Stage II Colon Cancer in Brazil − a Single Institution Experience

L.C.M. Aquino[1], B.S.V. Pereira[1], R.A. Gil[1], I.M. Oliveira[2], I.A. Small[3], J.C. Casali-da-Rocha[4], R. Moreira[4], C.G. Duque[1]. *[1]Instituto Nacional de Câncer − INCA, Oncology, Rio de Janeiro, Brazil; [2]Instituto Nacional de Câncer − INCA, Pathology, Rio de Janeiro, Brazil; [3]Instituto Nacional de Câncer − INCA, Clinical Research, Rio de Janeiro, Brazil; [4]Instituto Nacional de Câncer − INCA, Tumour Bank, Rio de Janeiro, Brazil*

Background: As stage II colon cancer patients may have a good outcome and adjuvant chemotherapy in this setting is controversial, the aim of the present study was to determine the clinical outcome of patients treated in a public institution from Brazil.
Patients and Methods: The tumour registry at National Institute of Cancer from Brazil was searched to identify patients with stage II colon cancer who underwent resection between January 2000 and December 2005. Data from 162 consecutive patients were collected using a standardized procedure. The Pearson Chi-square test and the Kaplan–Meier method were used.
Results: The median age at diagnosis was 62 (24−90); 45% were man; 35% reported a family history of colorectal cancer; 26% had a preoperative CEA >10 ng/mL. The mean time between diagnosis and surgery was 85 days. Intestinal obstruction and perforation were reported in 11.8% and 3.8% of patients, respectively. The pathological staging (AJCC 6º ed) was IIB (T4) in 79.6% and among these, invasion of other organs or structures was reported in 16% (22 patients). In 6.3% the tumour grade was poorly differentiated; 24% and 11% had vascular and perineural invasion, respectively. The mean number of lymph nodes examined in each specimen was 24. Adjuvant chemotherapy was indicated for 58 patients (35.8%). The mean time between surgery and initiation of adjuvant chemotherapy was 60 days. The regimen of treatment was bolus fluorouracil plus leucovorin, either a monthly 5-day course or a weekly 1-day course. Age less than 75 years (p < 0.002) and tumour invasion or adherence to other organs or structures (p < 0.001), but not histological grade, perforation or less than 12 nodes sampled, were significantly associated with the administration of adjuvant chemotherapy. With a median follow up of 67 months, the progression free survival at 3 and 5 years was 96.7% and 95.2%, respectively. Five years overall survival was 90.9%.
Conclusions: Most patients in this Brazilian cohort did not receive adjuvant chemotherapy, with age at diagnosis and tumour invasion the most frequent determinants. Efforts should be done to reduce the interval between diagnosis and surgery and the time to initiation of adjuvant treatment. Progression free and overall survivals were comparable with reported literature data.

6103 POSTER

Oxaliplatin and Capecitabine (CAPOX) in Non Selected Patients With Metastatic Colorectal Cancer (MCRC) After First-line Irinotecan Based Regimen

P.J. Fonseca[1], P. Solis[2], J.M. Vieitez[1], M. Izquierdo[1], P. Pardo[1], E. Gutierrez[1], Q. Pérez[1], C. Álvarez[1], M. Frunza[3], E. Uriol[1]. *[1]University General Hospital of Asturias, Medical Oncology, Oviedo, Spain; [2]Instituto Universitario de Oncología del Principado de Asturias (IUOPA), General Physician, Oviedo, Spain; [3]University General Hospital of Asturias, Surgery, Oviedo, Spain*

Background: It has not yet been established the best second line chemotherapy for MCRC although some studies suggest a better role for oxaliplatin after irinotecan than for irinotecan after oxaliplatin. We analysed if our data could be comparable to those of Tournigand, et al (JCO2004; 22:229).
Patients and Methods: This is a unicentric retrospective study including patients with MCRC who received CAPOX after progression to front-line treatment which initially was irinotecan, fluorouracil and leucovorin (IFL) and since 2005 with low dose capecitabine, irinotecan (CAPIRI) and bevacizumab in patients without contraindications to receive the targeted agent. The primary endpoint was overall survival (OS) and the second ones were response rate (RR), progression-free survival (PFS) and the safety profile.
Results: Between February 2002 and September 2010, 138 evaluable patients from a Spanish Medical Oncology Department were enrolled. Patients and treatment's characteristics are displayed in table 1.
The median OS was 7.85 months (95% CI, 6.73–8.97). The RR, the tumour growth control rate and the progression rate was 16%, 51% and 49%, respectively. The median PFS were 3.5 months. The median number of cycles received were 5 (limits: 1−24). Most frequent treatment-related grade 3−4 toxicities were diarrhea (9%), vomiting (6%) and asthenia (4%). 7% of