Results: 42 patients were accrued. Prior therapies included surgery (36%), radiofrequency ablation (7%), transarterial therapy (50%); prior systemic therapies (38%). Median follow-up was 20.0 months. Median cycle no. was 2 (range: 1−12). The PR and SD rate was 2.4% (1/42) and 45.2% (19/42) respectively. Median PFS was 2.64 months (95%C.I. 1.55–3.17) and OS was 6.60 months (95%C.I. 4.53–11.60). Grade ⩾3 toxicities that occurred in ⩾5% included: 4 (9.5%) abdominal pain, 4 (9.5%) hyperbilirubinemia, 4 (9.5%) raised alanine transaminase, 3 (7.1%) anemia, 3 (7.1%) vomiting, 2 (4.8%) distension, 2 (4.8%) hemorrhage, 2 (4.8%) prolonged QTc and 2 (4.8%) dehydration. One patient developed sudden death but it was determined not likely due to study medication.
Conclusions: With the majority of patients having failed prior therapy, epigenetic therapy with belinostat demonstrates tumour stabilization and is generally well-tolerated. Further studies including combinational study with other agents is warranted.
Acknowledgement: The study was sponsored by the Division of Cancer Treatment and Diagnosis, National Cancer Institute, U.S.A, and its collaborator TopoTarget.

6598 POSTER

Combination of Capecitabine and Oxaliplatin (CAPOX) is an Effective Option for the Treatment of Neuroendocrine Tumours (NET)

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Background: The role of chemotherapy in advanced NET is questionable. While carcinoid tumours are resistant to cytotoxic chemotherapy, streptozocin-based regimens are acceptable for treatment of pancreatic NET. Recently, it was demonstrated that Everolimus and Sunitinib have activity in low and intermediate grade advanced pancreatic NET, with a median progression free survival of 11 months and partial response rate (PR) between 5% and 9%. The aim of this retrospective analysis was to evaluate the activity of the CAPOX combination in treating NET in an unselected population.
Material and Methods: We retrospectively evaluated 24 patients diagnosed with metastatic NET treated with CAPOX at two Brazilian institutes that are reference in cancer care.
Results: Median age at diagnosis was 56 years (range 23 to 73), 71% were male, 71% had ECOG 0 or 1, 63% tumours were primary from pancreas, 17% lung, 8% small intestine, 4% rectum, 8% unknown primary and 29% were functional. According to WHO classification criteria, 25% were grade 1, 37.5% grade 2 and 37.5% grade 3. Local treatments as embolization, chemoembolization or hepatic surgery were performed in 29% of patients. Most patients received CAPOX in 2nd line (1st to 4th line), with a median of 6 cycles. 29% of patients had PR by RECIST criteria. No association was observed between response rate and tumour grade, primary site or line of CAPOX. The median time to progression was 9.8 months and median time to treatment failure was 12.1 months. 75% patients remain alive, so median overall survival was not reached. Toxicity grade 3 was observed in 21% of patients, mainly neuropathy and hand-foot syndrome. Dose reduction was necessary in 33% patients, but only 1 discontinued treatment due to toxicity.
Conclusions: The CAPOX combination is active in an unselected population with metastatic NET and may be a good platform for the incorporation of the newer molecular targeted agents being investigated for the treatment of NET.

6599 POSTER

Phase II Trial of Gemcitabine and an Omega-3 Rich Lipid Infusion in Advanced Pancreatic Cancer

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Background: Omega-3 fatty acids (n-3FA) have been shown to reduce cell proliferation and viability and induce apoptosis in pancreatic cancer cell lines and xenograft models. Oral preparations in human trials have shown mixed results but display a trend towards stabilisation of tumour-related cachexia and improved quality of life. Poor compliance and bioavailability of oral preparations is a recurrent problem. Novel biological agents which significantly improve survival, radiological response, quality of life (QOL) and tumour cachexia are currently unavailable.
Materials and Methods: A phase II single-arm (Simon's two-stage design) trial of gemcitabine (1000 mg/m3 weekly for 3 weeks followed by a rest week) plus intravenous n-3FA rich infusion (up to 100g, Lipidem ®, BBraun Melsungen) was administered to patients with histologically proven locally advanced or metastatic pancreatic cancer. Inclusion criteria were identical for single-agent gemcitabine. Historical data from a matched cohort of 24 patients receiving single-agent gemcitabine prior to trial initiation were obtained. Tumour assessment by RECIST criteria on CT was performed every 2 cycles. CA19-9 at baseline and every 2 cycles was measured. Primary outcome measure was objective response rate, with secondary outcome measures of overall and progression free survival, changes in QOL, weight and pain scores. Adverse events were recorded by CTCAE V4.0 criteria. The trial is registered with clinicaltrials.gov: NCT01019382 and sponsored by University Hospitals of Leicester.
Results: Twenty-six patients underwent 76 cycles (median = 3) of treatment, with 20 evaluable for response. 11/20 (55%) had liver metastases (LM) and 18/26 (69%) were male. Partial response (PR) rate was 3/20 (15%) overall and LM PR rate was 6/11 (55%). Disease control rate (best response of Stable Disease+PR) was significantly better in the n-3FA+gemcitabine group than historical controls: 15/20 vs 6/17 ($p = 0.002$). Mean change in overall target lesion and LM diameters was −12% (95% CI −2 to −23%) and −19% (95% CI −47 to +9%) respectively. Mean peak change in CA19-9 was −48% (95% CI −21 to −76%). Median overall survival and progression free survival (experimental group vs historical controls) was 6.0 vs 4.1 months ($p = 0.44$) and 3.6 vs 2.3 months ($p = 0.02$) respectively. Grade 3 or 4 thrombocytopaenia and neutropaenia rates were 16% and 8% respectively.
Conclusions: n-3FA rich lipid infusions in combination with gemcitabine may have activity in advanced pancreatic cancer. A phase III double blind randomised controlled trial is planned to assess this activity further.

6600 POSTER

A Randomized, Multicenter, Open-label, Phase III Study to Compare the Efficacy and Safety of Capecitabine Plus Paclitaxel Followed by Capecitabine Maintenance (PX-X) With Capecitabine Plus Cisplatin (XP) as a First-line Chemotherapy for Recurrent or Metastatic Gastric Cancer (PAC-C Study)

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Background: Our previous open label, phase II, multi-center prospective study (ML20312) has shown the efficacy and safety of paclitaxel plus capecitabine with subsequent capecitabine maintenance (PX-X) as first-line treatment for advanced gastric cancer (AGC). In this randomized, phase III, multi-center prospective study (PAC-C study), we would like to confirm the efficacy and safety of PX-X in treatment of AGC by comparing it with that of standard regimen of cisplatin/capecitabine (XP).
Methods: The study is registered with ClinicalTrials.gov ID of NCT01015339. Patients with previously untreated metastatic or recurrent gastric adenocarcinoma, signed informed consent, evaluable lesion(s) by RECIST 1.0, KPS⩾70 and adequate organ functions are eligible. No prior taxanes, or more than 2 cycles of capecitabine, or more than 300 mg/m^2 total dose of cisplatin is allowed in adjuvant or neoadjuvant chemotherapy. All eligible patients are randomized to 2 arms, PX-X or XP. In PX-X arm, Paclitaxel is given with 80 mg/m^2 for 3-hour infusion on day 1, 8, capecitabine is given with 1000 mg/m^2 twice daily day 1−14 (every 3 weeks) until progression/intolerance, or maximum 4 cycles. Subsequently, the patients with no progression were given maintenance therapy of capecitabine monotherapy with same dose/schedule as the combination therapy until progression or intolerance. In XP arm, cisplatin is given with 80 mg/m^2 for 2-hour infusion on day 1, capecitabine is given same to PX-X arm, until progression/intolerance, or maximum 6 cycles. The primary endpoint is progression free survival (PFS), and secondary endpoints are Disease Control (DCR), overall response Rate (ORR), overall survival (OS), safety, quality of life (QoL) and biomarker detection of TP, DPD, TS and β-tubulin. Our predicted PFS in PX-X arm is 6.5 months, the PFS in XP arm is 4.5 months according to China clinical practice in recurrent/metastatic gastric cancer treatment. 160 patients per arm was needed to provide an 80% chance of observing a difference of 2 months in PFS at significance level of 0.05. The patients will be followed up for 1 year after treatment end of last patient or death occurred in 75% patients. The protocol was amended in April, 2011 to include an interim safety analysis at the time of 160 patients enrolled.

Results: This study remains on schedule from Nov. 2009 to Mar. 2011. In 23 centers, 157 patients have been screened with 1 screen failure. Interim analysis will be done in Jun 2011, the enrollment is planned to be completed in Apr 2012. Up to now, 20 patients withdrew from the study, with 1 of capecitabine allergy, 2 of paclitaxel allergy, 4 of consent withdrawn, 2 of withdrawn after randomization, and 11 lost follow-up. Severe adverse event (SAE) is reported in 9 cases (cut-off date 31 Jan, 2011), 1 of multiorgan dysfunction syndrome (MODS), 2 of intestinal obstruction, 1 of liver dysfunction, 1 of hemorrhage, 1 of bone marrow failure, 1 of thrombosis, 1 of paclitaxel allergy, and 1 of diarrhea. One treatment-related death was suspected in all patients. Safety data is now under collection for interim safety analysis.
Conclusion: PX-X as first-line treatment was promising in AGC. Interim safety results and primary efficacy analysis are eagerly awaited.

6601 POSTER

Oxaliplatin, Leucovorin and Fluorouracil for Untreated Recurrent or Metastatic Esophageal Carcinoma − a Phase II Study

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Background: Esophageal carcinoma is one of the most common cancers, as well as one of the leading causes of cancer death in China. In Western countries, clinical trials are now primarily focusing on the treatment of adenocarcinoma, owing to the recent increase in the prevalence of this type of esophageal cancer. In China and other eastern Asian countries, squamous cell carcinoma is the main type of esophageal cancer. Monotherapy with oxaliplatin or 5-Fu has been demonstrated anticancer activity in esophageal cancer. This study was designed to evaluate the efficacy and toxicity of oxaliplatin, leucovorin and fluorouracil (FOLFOX6) in untreated recurrent or metastatic esophageal carcinoma.
Materials and Methods: Patients with recurrent or metastatic esophageal cancer ineligible for definitive radiotherapy were given FOLFOX6:oxaliplatin 100 mg/m^2, leucovorin 400 mg/m^2, fluorouracil (400 mg/m^2) as an i.v. bolus, fluorouracil (2400 mg/m^2) as a 46-h continuous infusion on day 1. Treatment cycles were administered every 14 days. The primary end point was progression-free survival (PFS). Secondary end points included objective response (OR), overall survival (OS) and safety.

Table 1. Adverse effects of 40 patients treated with FOLFOX6

Adverse effect	Number of patients				
	Total, N (%)	Grade 1	Grade 2	Grade 3	Grade 4
Leukopenia	32 (80%)	10	12	8	2
Neutropenia	28 (60%)	7	9	9	3
Anemia	22 (55%)	16	3	3	1
Thrombocytopenia	11 (27.5%)	3	5	3	0
Neuropathy	25 (62.5%)	23	2	0	0
Nausea	24 (60%)	18	5	3	0
Vomiting	15 (37.5%)	12	3	0	0
Stomatitis	25 (62.5%)	21	4	0	0
Diarrhea	5 (12.5%)	5	0	0	0
Fatigue	30 (75%)	20	8	3	0
Alopecia	8 (20%)	8	0	0	0
Hyperbilirubinemia	3 (7.5%)	3	0	0	0
Elevation of AST/ALT	5 (12.5%)	5	0	0	0

Results: Between Oct, 2008 and Dec, 2010, a total of 40 patients with median age of 56 years old were enrolled. Baseline characteristics: male/female: 35/5; squamous/adenocarcinoma: 36/4; surgery/radiotherapy/neoadjuvant or adjuvant chemotherapy: 26/17/16; metastasis: 1 site:5 pts, 2 sites:11 pts, 3 sites:10 pts, 4 sites:12 pts, 5 sites:2 pts; mediastinal lymph node(LN) metastasis(M): 29pts,supreclavicular LN M: 21pts,retroperitoneal LN M: 17pts,liver M: 15pts,lung M: 10pts,anastomotic recurrence: 9 pts,soft tissue M: 5 pts, bone M: 5pts,gastric M: 4pts,cervical LN M: 3pts. Median cycles of FOLFOX6 were 4. PR: 17.5% (7/40),SD: 45% (18/40),PD: 32.5% (13/40),unassessable: 5% (2/40). With median follow up of 10 months, twenty-four patients died. Median PFS was 5.8 months(95% CI: 4.1−7.5). Median survival was 8.5 months (95% CI: 7.1−9.8). FOLFOX6 was well tolerated. Adverse effects were listed in table 1.
Conclusion: Chemotherapy with FOLFOX6 for untreated advanced esophageal cancer had promising efficacy and good tolerance. It is worthy being test further.

6602 POSTER

Immune Therapy Targeting for HER2 in Esophageal Squamous Cell Carcinoma

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Background: In spite of the combined modality therapy, the prognosis with advanced esophageal squamous cell carcinoma (ESCC) patients remains poor. On the other hand, cytotoxic T lymphocytes (CTL) therapy and molecular targeting therapy for HER2 were effective in a variety of tumours. These therapies are therefore an attractive approach as a novel immune-adjuvant therapy for ESCC patients. To examine the possibility of these therapies for ESCC patients, we investigated the HER2 expression in ESCC patients, the effect of molecular targeting therapy for HER2 in ESCC cell lines and MHC class I expression in ESCC patients as tumour-antigen specific CTL recognize peptide epitopes on MHC class I.
Materials and Methods: We assessed the HER2 expression in ESCC patients (n = 85) and ESCC cell lines (n = 9) by HercepTest and Fluorescence in situ hybridization (FISH). We also assessed the MHC class I expression in ESCC patients (n = 80) by immunohistochemistry with anti-MHC class I monoclonal antibody. In a panel of ESCC cell lines, the effects of Herceptin and Lapatinib on anti-proliferative effect and apoptosis-inducing activity was evaluated, furthermore, the accumulation of HER2 on cell surface by Lapatinib and the combined effect of Lapatinib together with Herceptin on cell-mediated cytotoxicity were evaluated.
Results: In ESCC patients, FISH positive; 9.4%, HercepTest 2+/3+; 11.8% and HercepTest 1+; 17.6%. The down-regulation of MHC class I expression was observed in 38.7%, furthermore, there was a significantly inverse correlation of HER2 overexpression (FISH positive) with MHC class I expression ($\chi 2$ test p = 0.002). One ESCC cell line expressed HercepTest 3+ and FISH positive. Herceptin and Lapatinib inhibited cell proliferation and induced apoptosis in ESCC cell lines and Lapatinib induced greater effectiveness. Lapatinib caused the surface accumulation of HER2 in all ESCC cell lines and increased Herceptin-mediated antibody-dependent cell-mediated cytotoxicity by 15−25% with 3 ESCC cell lines including a HER2-overexpressing cell line and two non-HER2-overexpressing cell lines.
Conclusions: Although HER2 overexpressing ESCC patients are not so good candidates for CTL therapy because HER2 overexpressing ESCC cells reduced their sensitivity for CTL by MHC class I down-regulation, Herceptin and Lapatinib have activity in HER2 expressing ESCC cells and the combination therapy of Herceptin and Lapatinib is a promising strategy in ESCC.

6603 POSTER

Prognostic Factors of 127 Patients With Advanced Small-bowel Adenocarcinoma Treated With Systemic Chemotherapy

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Background: No standard care has been established for advanced small-bowel adenocarcinoma (SBA). The aim of this retrospective study is to explore a most promising chemotherapy regimen for advanced SBA after adjusting the background factors by multivariate analysis.
Methods: The subjects were 132 patients with advanced SBA who were treated by chemotherapy. Main inclusion criteria were 1) histologically proven SBA excluding ampullary carcinoma, 2) no previous chemotherapy or radiotherapy, 3) ECOG PS 0−2. Patients were classified into the following 5 groups according to the first-line chemotherapy: A) FU alone; B) FU + CDDP; C) FU + Ox; D) FU + CPT-11; E) others. Progression free survival (PFS) and overall survival (OS) were compared with the log-rank test, and every hazard ratio (HR) was calculated using univariate and multivariate analysis with Cox's proportional hazards model.