in 85 (44.9%) patients, proximal subtotal resection in 16 (8.5%) and distal subtotal resection in 75 (39.7%). Combined operations were performed in 58 (30.7%) patients. Control group formed 70 gastric cancer patients younger than 35 years old, who were performed variety kind operations.
Results: General postoperative complications developed in 39 patients (8.6%), and postoperative mortality was 8.9% in the main group. In control group complications developed in 5 (7.1%) patients and died 2 (2.8%) patients. Analysis of the remote results depending on the character of operation has shown that after radical operation 3-years survival rate was 40.9±3.5%, 3-years survival rate after palliative surgery was 20.8±3.5% in the main group. 3-years survival after radical operation was 45.0±4.3%, after radical curative surgery 3-years survival rate was 26.6±4.3% after palliative surgery in the control group.
Conclusion: Analysis the direct results of surgical treatment of gastric cancer patients in older age shows that, as a whole at the expense of numerous accompanying pathologies and decrease regeneration functions, the postoperative complications remain rather high and requires realization special methods of preparation. The satisfactory remote results of surgical treatment of gastric cancer patients in older age, in comparison with control group give the basis to perform radical surgery.

6556 POSTER

Splenic Artery Invasion in Pancreatic Adenocarcinoma of the Body and Tail − a Novel Prognostic Parameter for Patients Selection

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Background: The value of splenic vessels invasion (which identified T3 tumours) in prognosis after resection for pancreatic ductal adenocarcinoma (PDA) of the body and tail has been scarcely investigated. Aim of this study was to evaluate prognostic factors in PDA of the body/tail, emphasizing the role of splenic vessels infiltration.
Methods. Between 1990 and 2008, 87 patients who underwent distal pancreatectomy (DP) for histologically proven PDA of the body and tail were analyzed. Clinico-pathological prognostic factors for survival were evaluated. Univariate and multivariable analyses were performed.
Results. Postoperative morbidity was 31% with no mortality. The 1-, 3- and 5-year overall survival rates were 77%, 48% and 24.5%, respectively. Invasion of the splenic artery (SA) was observed in 19 patients (22%). All 19 patients with SA invasion had also SV involvement. The sensitivity and specificity of preoperative imaging in detecting SA infiltration resulted 37% and 96%, respectively. Patients with SA invasion had a significantly worse prognosis compared with those without SA invasion (median survival: 15 vs. 39 months, p = 0.014) (Figure). Of the 19 patients with SA infiltration, 17 had a recurrence. In all those 15 patients with SA involvement who died, 14 (93%) died within 2 years from surgery. Also patients with SV invasion had a poorer survival respect of patients without SV invasion (24 vs. 44 months, $P = 0.03$). On multivariable analysis, adjuvant therapy, poorly differentiation (G3/G4), R2 resection, the presence of lymph node metastases, and SA invasion were independent predictors of survival.
Conclusions. Invasion of SA is an independent predictor of poor survival in PDA of the body/tail. PDAs with SA invasion should be classified as T4 tumours rather than T3. The SA involvement implies a more aggressive tumour biology, although a radical resection can be achieved safely by a surgical standpoint. In the presence of SA infiltration, neoadjuvant treatment should be considered.

6557 POSTER

Pancreatic Endocrine Carcinoma − Lymph Node Ratio and KI67 Are Predictors of Recurrence After Curative Resections

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Introduction: Pancreatic endocrine carcinomas (PECs) are generally associated with a good prognosis after radical resection. In other pancreatic malignancies predictors of recurrence and the role of lymph node ratio (LNR) are well known, but both have been scarcely investigated for PECs.
Methods: The prospective database from the surgical Department of Verona University was queried. Clinical and pathological data of all patients with resected PECs between 1990 and 2008 were reviewed. Univariate and multivariate analysis were performed.
Results: Fifty-seven patients (male/female ratio = 1) with a median age of 58 years (33−78) entered in the study. Overall, 29 (51%) patients underwent pancreaticoduodenectomy and 28 (49%) distal pancreatectomy. Postoperative mortality was nil with a 37% morbidity rate. There were 36 (63%) patients with node metastases (N1). Patients with positive nodes had a lymph node ratio (LNR) $\leqslant 0.20$ in 44 cases whereas 13 (23%) had a LNR >0.20. The median overall survival and the median disease free survival (DFS) were 190 and 80 months, respectively. Recurrent disease was identified in 24 patients (42%) with a 2 and 5-year DFS rate of 82% and 49%, respectively. On multivariate analysis, LNR >0.20 (HR = 4.98) and a value of Ki67 >5% (HR = 2.75) were significant predictors of recurrence ($P < 0.03$).
Conclusions: After resection for malignant PECs, LNR and a Ki67 >5% are the most powerful predictors of recurrence. The presence of these factors should be considered for addressing patients to adjuvant treatment in future clinical trials.

6558 POSTER

Analysis of the N Descriptors and Other Prognosis Factors in Curatively Resected Thoracic Esophageal Squamous Cell Carcinoma

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Background: The seventh edition of the tumour, node, metastasis classification of esophageal cancer have been published. Different from the sixth edition, N descriptors are divided into N0, N1a, N1b, N2 and N3. We combined this new parameter with other well-established prognostic factors and performed multivariate survival analyses to validate its value in Chinese thoracic esophageal squamous cell carcinoma (TESCC).
Methods: We try to validate the new staging project in 1002 patients who underwent complete surgical resection (R0) for TESCC in single institution of Zhejiang Cancer Hospital from 2003 to 2008. Patients who received preoperative chemotherapy and/or radiotherapy were excluded. Variables in the analysis included age, gender, tumour location, local tumour stage, degree of cell differentiation and the stage of pN or vascular involvement, adjuvant chemotherapy and adjuvant radiotherapy. Survival curves were estimated using the Kaplan–Meier method and compared by the log-rank test. Multivariate analysis was performed by Cox regression model. Statistical analysis was performed using SPSS software, Version 13.0 (SPSS Inc., Chicago, IL). All probability values were two-sided and p values <0.05 were considered statistically significant.
Results: The median overall survival (OS) of different pN+ (pN1a, pN1b, pN2 and pN3) were 41.1, 21.3, 16.1 and 12.8 months respectively ($X2 = 57.91$, $p < 0.001$). The 5-year OS rate of patients with different pN+ (pN1a, pN1b, pN2 and pN3) were 43.7%, 25.0%, 14.4% and 11.8% respectively. The 5-year disease-free survival rate of patients with different pN+ (pN1a, pN1b, pN2 and pN3) were 37.8%, 24.1%, 11.4% and 3.8% respectively ($X2 = 60.09$, $p < 0.001$). Variables associated with worse OS on univariate analysis were male, length of tumour $\geqslant 5$ cm, deeper depth of invasion, more lymph node metastasis, higher histologic grade, vessel involvement positive, postoperative radiotherapy and postoperative chemotherapy. By multivariate analyses, gender (HR 0.54; 95% CI 0.37–0.80; p = 0.002), depth of invasion (HR 1.42; 95% CI 1.22–1.67; p < 0.001), histologic grade (HR 1.17; 95% CI 1.01–1.36; p = 0.040), and the stage of pN (HR 1.48; 95% CI 1.37–1.60; p < 0.001) were independent predictive factors for OS.
Conclusions: pN stage in the 7th edition is a significant independent prognostic factors in patients after curative surgery in Chinese TESCC.

6559 POSTER

Changes in Treatment for Advanced Carcinoma of the Biliary Tract With Cetuximab

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Background: The role of chemotherapy in advanced carcinoma of the biliary tract is limited. While resistance to cytotoxic chemotherapy may vary according to tumour location in the biliary tree, the value of cisplatin containing regimens was confirmed in a large prospective randomized trial and has become the standard of care for treatment for advanced carcinoma of the biliary tract. The recent addition of cetuximab to cisplatin-containing regimens has resulted in increased response rates in a phase II trial. A randomized phase II trial is now completed.
Material and Methods: We retrospectively evaluated all 37 patients diagnosed with advanced carcinoma of the biliary tract referred to a single clinical practice in a Brazilian Cancer Center from January 2005 to March 2011.

Results: Median age at diagnosis was 61 years (range 33 to 88), 67.6% were male, 86.4% had ECOG 0 or 1, 64.8% tumours were intrahepatic, 24.3% were from gallbladder and 10.8% were Klatskin carcinomas. According to tumour grading, 18.9% were well differentiated, 35.1% were moderately differentiated, 24.3% were poorly differentiated and 21.6% was not informed. All 37 patients were recommended palliative systemic therapy as primary treatment with cisplatin (or oxaliplatin) plus gemcitabine regimen until progression or death. Cetuximab was added to the chemotherapy regimen of 13 patients since May 2009. Overall, 28 (75.6%) patients were followed until death with a median follow-up of 9.2 month. Nine (24.3%) patients are still on therapy, 8 of them are still using cetuximab containing therapy, with a median follow-up of 24.4 months. The median overall survival of patients receiving cetuximab was not reached and it is significantly longer than the median overall survival of patients who never received cetuximab (9.2 months; 95% CI 3.5–12.3) (p = 0.0105, two sided log rank test).
Conclusions: In this retrospective analysis, the introduction of cetuximab in combination with cisplatin-containing chemotherapy regimens seems to improve survival of patients diagnosed with advanced carcinoma of the biliary tract. The completed randomized phase II trial may confirm the precise role of cetuximab in this disease once data is available. Due to rarity of this patient population and limitations of efficacy of current therapies, patients' referral to prospective phase III trials should be a high priority.

6560 POSTER

A Phase I Safety and Pharmacokinetic Study of Everolimus, an Oral mTOR Inhibitor, in Subjects With Impaired Hepatic Function

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Background: Everolimus, an oral mTOR inhibitor that demonstrates effective antitumour activity in several human tumours, is metabolized through the hepatic CYP450 pathway. Everolimus safety and pharmacokinetics (PK) in the setting of mild to severe hepatic impairment (Child-Pugh A, B, and C, respectively) has not been reported. This study assessed PK and safety of everolimus in pts with different degrees of hepatic impairment. The relationship between PK parameters and hepatic function was also investigated.
Materials and Methods: (ClinicalTrials.gov NCT00968591) Pts $\geqslant$18 years of age were assigned to 1 of 4 treatment groups: group 1 (normal hepatic function); group 2 (Child-Pugh A; score 5−6); group 3 (Child-Pugh B; score 7−9), or group 4 (Child-Pugh C; score 10−15). Pts received a single 10-mg dose of everolimus after a low-fat breakfast. PK parameters were determined by a validated noncompartmental analysis method using WinNonlin® Pro (Version 5.2).
Results: 34 pts (group 1, n = 13; group 2, n = 7; group 3, n = 8; group 4, n = 6) were evaluable for PK and safety. Baseline demographics were similar across groups (median age 44 years, male 79.4%, white 91.2%). Mean C_{max} and t_{max} of everolimus were comparable between normal or hepatic-impaired pts. Postabsorption-phase kinetics were notably different in normal vs hepatic-impaired pts. Compared to normal controls, there was a 1.6-fold, 3.26-fold, and 3.64-fold increase in everolimus $AUC_{(0-inf)}$ for patients with mild, moderate, and severe hepatic impairment, respectively. Everolimus $AUC_{(0-inf)}$ correlated positively with bilirubin level ($r^2 = 0.54$) and INR ($r^2 = 0.65$); a negative correlation was observed with albumin ($r^2 = 0.56$). Post hoc analysis suggested dose adjustment based on bilirubin or albumin may result in over- and underdosing. Incidence of AEs was higher in groups 3 (n = 3) and 4 (n = 2) than in the control (n = 1) and group 1 (n = 1). The majority of AEs were grade 1 severity, $\leqslant$1 day in duration, and not everolimus related.
Conclusion: Hepatic impairment assessed by Child-Pugh class correlates with everolimus PK and should be used to guide dose adjustment in pts with hepatic impairment. For pts with mild or moderate hepatic impairment, the recommended starting dose of everolimus is 7.5 mg and 2.5 mg OD, respectively. Everolimus cannot be recommended for pts with severe hepatic impairment (Child-Pugh C) unless in the best interest of the pt; a starting dose of 2.5 mg OD must not be exceeded. Safety of everolimus was consistent with previous experience.

6561 POSTER

Updated Survival and Safety Data From RADIANT-3 − a Randomized, Double-blind, Placebo-controlled, Multicenter, Phase III Trial of Everolimus in Patients With Advanced Pancreatic Neuroendocrine Tumours (pNET)

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Background: Effective treatments for controlling disease progression in pts with advanced pNET are limited. Estimated median overall survival (OS) for treatment-naive pts with metastatic disease is 24 mo (Yao et al, 2008). In the largest randomized phase III study (RADIANT-3, NCT 00510068) in pts with advanced pNET, everolimus, an oral mTOR inhibitor, provided a statistically significant 2.4-fold improvement in progression-free survival (PFS) vs placebo (HR, 0.35; 95% CI, 0.27–0.45; $P < 0.0001$). Here we present an update of the survival and safety analysis from this trial.
Materials and Methods: Pts with progressive advanced low- or intermediate-grade pNET were randomly assigned to everolimus 10 mg/d orally (n = 207) or placebo (n = 203); both arms received best supportive care. Primary endpoint was PFS (RECIST v1.0). Upon disease progression, pts assigned to placebo could cross over to open-label everolimus. The updated OS analysis cutoff date was Feb 23, 2011 (143 events: 68 everolimus; 78 placebo). Adverse events (AEs) were coded to a preferred term and graded using the National Cancer Institute Common Toxicity Criteria (v3.0). The safety population included 407 pts (204 everolimus; 203 placebo).
Results: Of the 203 placebo pts, 172 (85%) crossed over to open-label everolimus; 124 of the 146 (58%) pts with disease progression crossed over to open-label everolimus during blinded study therapy. Median OS was 36.6 mo in the placebo arm and has not been reached in the everolimus arm (HR, 0.89; 95% CI, 0.64–1.23). Median PFS for pts who received open-label everolimus after disease progression was 11.43 mo. Median safety follow-up now extends to 20.1 mo. Most common drug-related AEs with everolimus vs placebo remained stomatitis (52.9% vs 12.3%), rash (48.5% vs 10.3%), and diarrhea (34.3% vs 10.3%). Anemia (5.9% vs 0%), hyperglycemia (5.9% vs 2.5%), and stomatitis (4.9% vs 0) were the most common drug-related grade 3/4 events for everolimus and placebo, respectively.
Conclusions: At 40 mo of follow-up, the median OS has not been reached in the everolimus arm. Median OS in the placebo arm, in which substantial crossover occurred benefitting these patients, exceeds the median previously observed for pts with metastatic pNET. The safety of everolimus observed in this analysis was consistent with previous experience. Final survival analysis will be completed after 282 events.
Study supported by Novartis.

6562 POSTER

Perioperative Chemotherapy in Resectable Gastric Cancer − a Single Centre Review

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Background and Objective: Perioperative chemotherapy (CHT) with epirubicin, cisplatin and infusional fluorouracil (ECF) has shown benefits in resectable gastric cancer, improving progression-free and overall survival. We reviewed the feasibility of perioperative CHT in our setting, as for the completion of the protocol and tolerability.
Material and Methods: Patients (pts) clinical files with gastric or gastroesophageal junction cancer submitted to perioperative CHT were reviewed from January 2009 to October 2010.
Results: Forty-two (pts) were treated, 33 male and 9 female, with a medium age of 66 years. The histological diagnosis was adenocarcinoma, with 2 cases of signet ring cells carcinoma and 8 cases of mucinous adenocarcinoma. All tumours were T $\geqslant$ 3 or N positive. Chemotherapy was based in ECF. In 10 pts, cisplatin was replaced for oxaliplatin due to polyneuropathy (1 pt), cardiac disease (6 pts) and hearing problems (1 pt). In 1 pt, fluorouracil was replaced for capecitabine due to catheter complications and in another patient epirubicin was