omitted because of compromised LEVF. Twenty six pts completed all protocol treatments (chemotherapy and surgery). Forty-one pts completed preoperative chemotherapy and underwent surgery. In 5 pts surgery was palliative, for unresectable or unsuspected metastatic disease. Reasons for not completing treatment were: disease progression (10 pts), postoperative complications (3 pts), prolonged neutropenia (1 pt), febrile neutropenia with septic shock and prolonged UCI stay (1 pt) and diverticulitis (1 pt). Dose reduction was required in 9 pts, due to diarrhea (3 pts), neutropenia (2 pts), neurotoxicity (1 pt), weight loss (1 pt), catheter complications (2 pt). Chemotherapy delay occurred in 23 pts (minimum 7 days − maximum 14 days), and the main causes were: delay in admission, neutropenia, diarrhea, and postoperative complication. With a medium follow up of 37 months, 7 pts died of progressive disease, two of them had completed full treatment.
Conclusion: Completion of all planned perioperative chemotherapy was observed in 71% of patients. Disease progression was the main reason to stop chemotherapy and although some pts were not able to receive post-operative treatment, tolerability was reasonable.

6563 POSTER

Chromogranine a (CG-A) Plus Vascular Endothelial Growth Factor (VEGF) as Predicting Factors (PF) of Sorafenib (SFB) Treatment of Multifocal Hepatocellular Carcinoma (M-HCC) in Elderly Patients

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Background: To date HCC accounts for approximately 90% of all primary liver cancers, this is the fifth most common cancer in the world with very poor prognosis. Despite treatment M-HCC outcomes are very discouraging and only sorafenib one of new TKI has demonstrated better effectiveness. Furthermore, till now we can only monitoring therapy effectiveness and prognosis with CT-Scan or Liver-Sonography or MRI.
Based on preliminary findings, authors will investigate if Cg-A and VEGF work as predicting factors of Sorafenib treatment's outcomes.
Material and Methods: 27 patients, mean age 68.6 (65−85) with M-HCC were observed and enrolled in this study in the last 24 months. Serum Cg-A (Chromogranin A ELISA), VEGF (Human VEGF ELISA) and αFP were evaluated at baseline and after end of treatment. SFB was delivered at standard dose of 400 mg p.o. bid and no one patients discontinued treatment for HFS and G.I.tract toxicity. Clinical response (RECIST), Comprehensive Geriatric Assessment and PFS were considered as well.
Results: Cg-A mean value was: (baseline) 78.7±9.0 ng/ml (after treatment) 25.59±9.0 ng/ml. VEGF levels was: (baseline) 65.8±8.7 pg/ml (after treatment) 48.33±8.7 pg/ml. Hand-Foot Syndrome and G.I. tract toxicity (grade 3−4) was not observed in these pts. Clinical benefit correlated with lower values of CgA and VEGF.
Conclusions: Both Cg-A and VEGF seem to be in reciprocal relation with response to SFB therapy in elderly with M-HCC patients. Further, a correlation between CT-Scan, Sonography and MRI of liver with prognosis of M-HCC was shown. A large number of patients are enrolling to convalidate these findings.

6564 POSTER

Correlation of PFS With Early Response of Chromogranin A and 5-hydroxyindoleacetic Acid Levels in Pts With Advanced Neuroendocrine Tumours: Phase III RADIANT-2 Study Results

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Background: In the phase III RADIANT-2 trial (NCT00412061; ESMO 2010 Abstract LBA8), everolimus 10 mg/d, an oral mTOR inhibitor, + octreotide LAR 30 mg IM q28 days (E+O) demonstrated a clinically meaningful 5.1-mo increase in median progression-free survival (PFS) compared with placebo + octreotide LAR (P+O) in pts with low- or intermediate-grade advanced NET and a history of flushing and diarrhea. Chromogranin A (CgA) and 5-hydroxyindoleacetic acid (5-HIAA) are important biomarkers of tumour burden and carcinoid syndrome in NET. Elevated vs nonelevated baseline CgA (11.3 vs 26.8 mo; HR, 0.45; $P < 0.001$) and 5-HIAA (13.6 vs 15.4 mo; HR, 0.79; $P = 0.130$) have been shown to be associated with shorter median PFS (WCGI 2011). This analysis examined the effect of baseline and early CgA and 5-HIAA response on PFS in the RADIANT-2 trial.
Materials and Methods: Pts with low- or intermediate-grade advanced NET were randomly assigned to E+O (n = 216) or P+O (n = 213). Primary endpoint was PFS (RECIST v1.0). Serum CgA and 24-h urinary 5-HIAA were collected at baseline and on day 1 of each cycle. Early CgA and 5-HIAA responses, defined as ⩾50% reductions at week 4, were correlated with PFS using a Cox-proportional hazards model.
Results: At baseline, 71.7% of E+O pts and 62.5% of P+O pts had elevated CgA (>2×ULN); elevated (>2×ULN) 5-HIAA was observed in 67.9% and 66.0%, respectively. The number of pts with early CgA (24.5% vs 16.5%) and 5-HIAA (24.0% vs 17.5%) responses were greater with E+O than P+O. Median PFS was significantly longer among pts with an early CgA response (27.3 vs 10.6 mo; HR, 0.35; $P < 0.001$) vs those without early response, regardless of treatment. Patients with early 5-HIAA response also had a longer median PFS than those without, but it did not reach statistical significance (18.3 vs 13.6 mo; HR, 0.71; $P = 0.139$).
Conclusions: In the large population of pts from the phase III RADIANT-2 trial, early CgA responses were associated with significantly improved PFS regardless of treatment, suggesting that early CgA response may serve as a surrogate for favorable PFS.
Study supported by Novartis.

Early response	Median PFS		Hazard Ratio	*P*
	E+O (N = 216)	P+O (N = 213)	E+O vs P+O	
CgA				
Yes	27.3 (13.9, NR) n = 34	27.8 (13.0, 30.4) n = 20	0.79 (0.4, 1.8)	0.283
No	13.7 (10.6, 16.1) n = 105	8.3 (5.9, 9.4) n = 101	0.54 (0.4, 0.8)	<0.001
5-HIAA				
Yes	18.3 (8.57, NR) n = 24	16.9 (8.4, 30.4) n = 18	0.81 (0.4, 1.8)	0.229
No	18.6 (13.6, 24.8) n = 76	8.4 (8.1, 13.6) n = 85	0.54 (0.3, 0.8)	0.003

NR, not reached.

6565 POSTER

Androgens in the Etiology of Esophageal Adenocarcinoma − a Population-based Cohort Study on Prostate Cancer Patients in Sweden 1961 to 2008

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Background: The incidence of esophageal adenocarcinoma is continuing to rise in western populations. There is a major male predominance, unexplained by sex differences in the distribution of known risk factors. Androgens may play a role in the etiology of esophageal adenocarcinoma and anti-androgen treatment might thus protect against the development of this tumour.
Material and Methods: The nationwide Swedish Cancer Register was used to identify a cohort of men diagnosed with a first malignant primary of prostate cancer, an androgen sensitive tumour often receiving hormonal therapy. All participants in the cohort were followed until a diagnosis of a second primary cancer, death, loss to follow-up or end of the study period. Age- and period adjusted standardized incidence ratios (SIR) with 95% confidence interval (CI) were calculated as an estimation of relative risk for a second malignant primary tumour of the esophagus.
Results: Between 1961 and 2008 190,497 patients developed cancer of the prostate as a primary malignant tumour in Sweden. Following exclusion for a follow-up period of less than one year 162,771 patients were eligible for study, contributing 712,496 person-years of follow-up. In total, 60 primary esophageal adenocarcinoma were observed in the cohort as compared to 62.1 expected, resulting in a SIR of 0.97 (95% CI 0.74−1.24).
Conclusions: The risk of developing esophageal adenocarcinoma following a diagnosis and treatment of a primary prostate cancer was no different than expected in the general population. Despite a large cohort our study was hampered by a small number of cases of esophageal adenocarcinoma and of misclassification of anti-androgen exposure diluting

possible differences toward zero. In summary, this study does not support but can neither fully refute the possibility of an association between androgens and the development of esophageal adenocarcinoma.

6566 POSTER

Updated Safety and Efficacy Results From RADIANT-2 − a Randomized, Double-blind, Multicenter, Phase III Trial of Everolimus + Octreotide LAR Vs Placebo + Octreotide LAR in Pts With Advanced Neuroendocrine Tumours (NET)

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Background: In the RADIANT-2 (NCT00412061), the largest phase III trial in advanced NET, treatment with everolimus + octreotide LAR (E+O) delayed disease progression by 5.1 months vs placebo + octreotide LAR (P+O) (Pavel ESMO 2010 LB8). However, imbalances in several important prognostic baseline factors favoring the P+O arm occurred.
Materials and Methods: Pts were randomized to everolimus 10 mg/d orally + octreotide LAR 30 mg IM q28d (n = 216) or to P+O 30 mg IM q28d (n = 213). Primary endpoint was PFS (RECIST v1.0). At the time of disease progression, pts randomly assigned to P+O could cross over to open-label E+O. At the time of this updated overall survival (OS) analysis (March 10, 2011), 223 events had occurred: 117 in E+O and 106 in P+O arms. Adverse events (AEs) were coded to a preferred term and graded using the National Cancer Institute Common Toxicity Criteria (v3.0). Safety population included 426 pts (215 E+O; 211 P+O).
Results: There was an imbalance between arms in poststudy anticancer treatments. Of the 213 pts assigned to the P+O arm, 143 (67.1%) crossed over to open-label E+O. In contrast, only 69 (32%) of E+O pts received subsequent therapy. Additionally, there was an imbalance in subsequent poststudy treatment with SSA favoring P+O arm. No significant differences were observed in median OS (HR, 1.17; 95% CI, 0.90–1.52). Adjusting for the imbalances in prespecified prognostic factors, HR =1.06 (95% CI, 0.81–1.39). Median safety follow-up now extends to 31.1 mo; updated safety data consistent with the original analysis. Common drug-related AEs (E+O vs P+O, %) were stomatitis (47.4 vs 10.9), rash (37.2 vs 12.3), and fatigue (31.6 vs 24.2). Most frequent drug-related grade 3/4 events were fatigue (6.5 vs 2.8), diarrhea (6.0 vs 2.4), hyperglycemia (5.1 vs 0.5), and thrombocytopenia (4.7 vs 0).
Conclusions: There were no significant differences in the ITT or the adjusted survival analysis between the two treatment arms. Final survival analysis will be completed after 252 events and likely will continue to be confounded by the crossover study design, imbalances in important prespecified baseline prognostic factors, and imbalances in poststudy anticancer therapies and SSA use. The safety profile of E+O was consistent with the primary study results and everolimus safety overall.
Study supported by Novartis.

6567 POSTER

A Phase II Trial of Erlotinib in Combination With Gemcitabine and Cisplatin for Unresectable Pancreatic Cancer

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Background: We performed a phase II study of erlotinib in combination with gemcitabine and cisplatin (GPT) for treating chemo-naïve patients with unresectable pancreatic cancer to evaluate the efficacy and toxicity.
Material and Methods: Patients were treated with erlotinib 100 mg daily, administered orally on days 1−21, and 1250 mg/m^2 of gemcitabine and 25 mg/m^2 of cisplatin administered via an intravenous infusion on days 1 and 8. The treatment was repeated every 3 weeks and continued until disease progression, withdrawal due to toxicity, or withdrawal of consent.
Results: Twenty-two patients were enrolled between June 2009 and August 2010. The median age of patients was 63 years (range, 32−73 years). Male to female ratio was 18:4. Reasons of unresectability were metastasis to other organ in 14 patients (63.6%), relapse in 5 patients (22.7%), or locally advanced inoperable 3 patients (13.6%). Median numbers of treatment was 4 cycles (range, 1−10 cycles). No complete response was observed and a partial response was observed in 5 patients (22.7%), Stable disease in 7 patients (31.8%), and progressive disease in 7 patients (31.8%). 3 patients did not disease evaluation. The median time to progression was 4.0 months (95% CI: 2.9−5.1 months), and the median overall survival was 6.8 months (95% CI: 3.7−9.9 months). Although the response rate in stage I reached the target ($\geqslant$ 3/22, p0=10%) established for movement to stage II, this study had to be discontinued because four patients had expired during treatment related with experimental drugs and the follow-up loss rate was higher (18.2%) than we had anticipated.
Conclusions: Even though erlotinib in combination with gemcitabine and cisplatin regimen is effective for unresectable pancreatic cancer, treatment related mortalities and high follow-up loss rate suggested this GPT protocol early closure and modification.
ClinicalTrials.gov Identifier: NCT00922896

6568 POSTER

DocOX − a Phase II Trial With Docetaxel and Oxaliplatin as a 2nd-line Systemic Therapy for Patients With Advanced And/or Metastatic Adenocarcinoma of the Pancreas − Interim Analysis

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Background: The ductal pancreatic adenocarcinoma is the fifth most common cause for cancer-related cases of death in Europe and the United States. For patients with a metastatic disease (UICC stadium IV), a cytostatic systemic therapy in palliative intention is the only treatment option.
At progressive disease under first-line chemotherapy it is often common to start a second-line systemic therapy with Fluoropyrimidine if applicable eventually in combination with Oxaliplatin. But actually there is no well-established standard for treatment in the second-line situation. There are well-known positive data about combination of Gemcitabine with Oxaliplatin and also of Gemcitabine with Docetaxel regarding to progression free survival (PFS) and tumour response in the palliative first-line situation.
For the first time, the DocOx-trial investigates the combination of Oxaliplatin with Docetaxel as an option for the second-line treatment option after progressive disease under palliative first-line cytostatic systemic therapy with Gemcitabine.
Methods: Prospective, single arm, non-randomized, multicenter, phase II trial with Docetaxel (75 mg/m^2, 60 min, d 1) plus Oxaliplatin (80 mg/m^2, 120 min, d 2, qd 22). Duration of trial is scheduled over 8 cycles maximum.
Primary endpoint: tumour response according to response evaluation criteria in solid tumours (RECIST). Secondary endpoints: PFS, overall survival (OS), safety/toxicity, quality of life/clinical benefit.
Interim analysis after inclusion of 22 patients (overall scheduled n = 44) in reference to tumour response and PFS.
Results: Among 22 patients included 2009 and 2010 50% (n = 11) had a stable disease (SD) at the first staging point (cycle 3, d 1), 5% (n = 1) had a partial remission (PR) and 41% (n = 9) a progressive disease (PD). At the second staging point (cycle 5, d1) of the remaining 11 patients 25% (n = 3) had a partial remission, 42% (n = 5) were stable (SD) and 25% (n = 3) showed a progress (PD). At the third staging point (cycle 7, d1) 6 patients were left, 17% (n = 1) with PR, 50% (n = 3) with SD and 33% (n = 2) showed a progressive disease.
In summary we saw a tumour response rate of 18% (n = 4, 95%-confidence interval 5.19–40.28%) among our patients and a progression free survival (PFS) of 14.3 weeks (3.57 month).
Conclusions: The results of our interim analysis fulfill the given requirements to proceed the DocOx-trial. Oxaliplatin plus Docetaxel as adjunction in the second-line treatment of pancreatic adenocarcinoma seems to be a possible therapeutic option.