doxorubicin produces a low response rate without survival benefit and well known toxicity; on the other hand single use of PLD has been reported to be safe and active against HCC. Gemcitabine is active against the most solid tumors. We evaluated the effectiveness of two drugs in combination; primary end points were median survival, median time to progression (TTP) and response rate while secondary end point included toxicity evaluation.
Patients and Methods: we enrolled 41 patients (PTS) with histological diagnosis of HCC not suitable for loco-regional treatment. Median age was 63.2 (range 44−78) years; male/female = 33/8; performance status (PS) = 0 in 36 PTS, PS = 1 in 4 PTS and PS = 2 in 1 PT. Twenty PTS had metastatic disease. Prior treatments were TACE in 13 PTS, PEI in 9 PTS, surgery in 12, RFTA in 6 PTS and chemotherapy in 3 PTS. Twenty PTS had Child-Pough A-B cirrhosis HBV-HCV related. PLD was administered at the dose of 30 mg/m^2 over a 60' infusion every 28 days and G at the dose 1,000 mg/m^2 over 30' infusion days 1 (immediately after PLD) and 8 every 28 days. Instrumental response evaluation was performed every 3 cycles and treatment was continued until progression or major toxicity.
Results: A total of 207 cycles were delivered (median for each patient = 4). Forty PTS were valuable for response with CR in 3, PR in 7, SD in 14 and PD in 16. In a patient with PR was performed a liver transplant. The median survival (calculating Kaplan-Meier) was 25.2+ (range 1.7−52.9+) months and the median TTP was 7.8+ (range 0.7−52.9) months. All PTS were evaluable for toxicity: G1−2 toxicity was neutropenia in 7 PTS, thrombocytopenia in 7, mucositis in 3 and PPE in 3. G3−4 toxicity was neutropenia in 7 PTS and thrombocytopenia in 4.
Conclusions: The combination of PLD and G is safe and effective in treatment of advanced HCC.

6621 POSTER

Effect of macroscopic vascular invasion (MVI), extrahepatic spread (EHS), and ECOG performance status (ECOG PS) on outcome in patients with advanced hepatocellular carcinoma (HCC) treated with sorafenib: analysis of two phase III, randomized, double-blind trials

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Background: The landmark Phase III SHARP trial showed that sorafenib is effective and safe for the treatment of advanced hepatocellular carcinoma (HCC) (Llovet et al, *N Engl J Med*, 2008). These results were confirmed in an Asian population in the Phase III Asia-Pacific (AP) study (Cheng et al. *Lancet Oncol*, 2009). MVI and EHS are predictive of poor prognosis, and ECOG PS significantly affects survival in patients with HCC. We performed subgroup analyses to evaluate the effect of MVI, EHS, and ECOG PS on the efficacy and safety of sorafenib in patients enrolled in the SHARP and AP trials.
Methods: Patients with advanced HCC, ECOG PS 0−2, Child-Pugh A, and no prior systemic therapy for HCC were randomized to sorafenib 400 mg BID or placebo (SHARP: N = 602; AP: N = 226). Patients in the AP study had more advanced disease and a predominance of hepatitis B infection. Endpoints included overall survival (OS), disease-control rate (DCR; defined as complete/partial response or stable disease by RECIST, maintained for ⩾28 days from first demonstration of response), and safety.

	n		OS (Sorafenib/Placebo)		DCR (%) (Sorafenib/Placebo)
Group	Sorafenib	Placebo	Median (mo)	HR (95% CI)	
SHARP					
Overall	299	303	10.7/7.9	0.69 (0.55, 0.87)	43.5/31.7
MVI/EHS	209	212	8.9/6.7	0.77 (0.60, 0.99)	41.2/27.8
No MVI/EHS	90	91	14.5/10.2	0.52 (0.32, 0.85)	48.9/40.7
ECOG 0	161	164	13.3/8.8	0.68 (0.50, 0.95)	46.6/36.0
ECOG 1/2	138	139	8.9/5.6	0.71 (0.52, 0.96)	39.9/26.6
AP					
Overall	150	76	6.5/4.2	0.68 (0.50, 0.93)	35.3/15.8
MVI/EHS	118	61	5.6/4.1	0.75 (0.54, 1.05)	30.5/11.5
No MVI/EHS	32	15	14.3/8.0	0.45 (0.19, 1.06)	53.1/33.3
ECOG 0	38	21	7.1/8.1	0.77 (0.42, 1.44)	39.5/23.8
ECOG 1/2	112	55	6.1/3.9	0.61 (0.42, 0.88)	33.9/12.7

Results: Efficacy results are shown in the table. The incidence of grade 3/4 drug-related adverse events (AEs) across subgroups in each study was consistent with the overall population for each study. The most common grade 3/4 AEs in all sorafenib populations were hand-foot skin reaction and diarrhea.
Conclusions: Sorafenib is effective and safe for the treatment of advanced HCC in patients globally, irrespective of baseline ECOG PS and presence or absence of MVI and/or EHS.

6622 POSTER

Primary extragastrointestinal stromal tumors in the omentum and mesentery: a clinicopathological and immunohistochemical study

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Background/Aims: This study aimed to describe the clinical, histological and immunohistochemical characteristics of primary extragastrointestinal stromal tumors (EGISTs) of the omentum and mesentery diagnosed in the Hospital 12 de Octubre, in Madrid, Spain, from 1993–2005.
Methodology: The clinical data and histological and immunohistochemical findings of primary mesenchymal neoplasias were revised using the Department of Pathological Anatomy databases.
Results: Six EGISTs were identified. Three were primarily of the omentum and 3 mesenteric. They were found in 4 males and 2 females with an average age of 65.16 years. All were c-KIT positive, and the majority CD34 positive, while 3 were positive for muscle-specific actin. The 3 omentum cases had a mixed spindle/epithelioid pattern and low mitotic rate, while the 3 mesenteric cases had a spindle pattern, with a high mitotic rate in 2 cases, where hepatic metastasis appeared at 6 and 32 months respectively. The 3 omentum cases were alive at the time of writing, and free of disease at 16, 21 and 34 months of follow-up. EGISTs represent 11.9% of GIST cases diagnosed in the hospital over the period 2000–2005.
Conclusions: In this study primary EGISTs of the omentum and mesentery showed clinicopathological and immunohistochemical characteristics similar to those previously in the literature for GISTs of the digestive tract, which supports the hypothesis that these tumors originate from extragastrointestinal c-KIT positive cells. Mesenteric location appears to be associated with a poorer prognosis.

6623 POSTER

Cisplatin plus etoposide as first-line chemotherapy for poorly-differentiated neuroendocrine carcinoma of the hepatobiliary and pancreatic region

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Background: The selection of treatment for neuroendocrine tumors depends on tumor grade, hormone hyper-secretion symptoms, and tumor extension. More specifically, since the biological behavior of poorly-differentiated neuroendocrine carcinomas (PD-NECs) is aggressive and similar to that of small-cell lung cancer (SCLC), one of the standard regimens for SCLC, combination chemotherapy consisting of cisplatin plus etoposide, has been widely used to treat PD-NEC, because no promising chemotherapy regimens have been reported for the hepatobiliary or pancreatic PD-NEC.
Material and Methods: We reviewed the cases in our database from October 1995 to January 2009 and retrospectively examined the clinical data of patients (pts) with unresectable or recurrent PD-NEC arising from the hepatobiliary and pancreatic region, who received cisplatin plus etoposide combination as first-line chemotherapy. The chemotherapy regimen consisted of cisplatin 80 mg/m^2 intravenously (IV) on day 1 and etoposide 100 mg/m^2 IV on days 1, 2 and 3, repeated every 3−4 weeks.
Results: Twenty-one pts were treated with the above regimen of cisplatin plus etoposide. The primary tumor site was the liver (2 pts), gallbladder (8 pts), pancreas (10 pts), and ampulla of Vater (1 pt). Although no complete response was seen, a partial response was achieved in 3 pts, resulting in an overall response rate of 14% (95% confidence interval, 3 to 36%). Median progression-free survival was 1.8 months and median overall survival was 5.8 months with the 1-year survival rate of 5%. The major grade 3 and 4 toxicities were leukopenia (71%), neutropenia (90%), nausea (33%) and anorexia (24%), and febrile neutropenia occurred in 8 pts (38%).
Conclusions: The cisplatin plus etoposide combination as first-line chemotherapy for PD-NEC of the hepatobiliary and pancreatic region had only marginal antitumor activity and had relatively severe toxicity compared with previously reported studies for extrapulmonary PD-NEC.