6.5 *v* 3.7 months (P = 0.004) and 12.5 *v* 9.0 months (P = 0.026), respectively. In a Cox multivariate analysis, AFP response (responders *v* non-responders; hazard ratio, 0.38; 95% CI, 0.226 to 0.649; P < 0.001) and performance status were identified as contributory prognostic factors for OS. AFP responses or normal AFP levels were observed in 40 of 77 patients with radiologically stable disease and identified a subset of patients with better PFS (8.7 *v* 6.0 months; P = 0.005) and OS (13.8 *v* 9.2 months; P = 0.025). In AFP responders and in patients with normal AFP levels, OS was similar (P = 0.3).
Conclusions: Evaluation of AFP decline is an useful and non-invasive prognostic tool for treatment monitoring in patients with advanced HCC treated with sorafenib.

6617 POSTER

Phase II study of NGR-hTNF, a selective vascular targeting agent (VTA), in previously treated patients (pts) with advanced hepatocellular carcinoma (HCC)

A. Santoro[1], G. Citterio[2], T. Pressiani[1], V. Gregorc[2], L. Rimassa[1], F.G. De Braud[3], G. Rossoni[2], F. Caligaris Cappio[2], A. Lambiase[4], C. Bordignon[4]. *[1]Istituto Clinico Humanitas, Department of Oncology, Milan, Italy; [2]Istituto Scientifico San Raffaele, Department of Oncology, Milan, Italy; [3]Istituto Europeo di Oncologia, Clinical Pharmacology and New Drugs, Milan, Italy; [4]MolMed, Clinical Development, Milan, Italy*

Background: HCC is a highly vascularised tumor with a median survival of 6 months reported in untreated pts with advanced disease class C according to Barcelona Clinic Liver Cancer (BCLC) staging. NGR-hTNF is a VTA consisting of TNF-a fused to the tumor-homing peptide NGR, which binds an aminopeptidase N overexpressed on tumor vessels.
Methods: Advanced-stage HCC pts received NGR-hTNF 0.8 μg/m^2 infused over 1-hour every 3 weeks (q3w). Progression-free survival (PFS) was the primary study aim with restaging performed q6w. A two-stage design was used with 16 and 27 pts to be enrolled. Subsequently, an additional 12 pts were treated with 0.8 μg/m^2 on a weekly basis (weekly cohort).
Results: Pts with documented progression after loco-regional treatments (59%), systemic therapies (56%; range, 1−3 regimens), or both (33%) received 90 cycles (range, 1−18+). Pt characteristics were: median age 65 years (range, 34−79); M/F 21/6; PS 0/1 18/9; Child-Pugh (C-P) A/B 21/6, BCLC B/C 5/22. No grade 3−4 drug-related toxicities were observed. Main grade 1−2 toxicities were short-lived, infusion-related chills (55%). The median PFS was 2.3 months (95% CI, 1.7−2.9). The disease control rate (DCR) was 30% and the confirmed response rate was 8%. A complete response (4%) lasting 11.5+ months was observed in a 76-year-old sorafenib-refractory, C-P B pt. A partial response (4%) with a 78% tumor reduction was reported in a further C-P B pt. Additionally, a 28% tumor shrinkage was detected in one out of 6 patients (22%) experiencing stable disease. Pts who achieved disease control received a median of 5 cycles (range, 4−18+) and had a median PFS of 4.3 months (range, 3.0−12.8+). With a median follow-up of 14.0 months (95% CI, 12.7−15.3), 8 pts (30%) were still alive and the median overall survival (OS) time was 9.1 months (range, 1.3−21.3+). The survival rates at 12 and 18 months were 34% and 22%, respectively. In the weekly cohort, there was no worsening of toxicity and the DCR was 33%. The subset of 12 sorafenib-pretreated pts reported a response rate of 8% and a DCR of 33%, whereas the median PFS and OS were 2.3 and 9.5 months, respectively.
Conclusions: NGR-hTNF is well tolerated and appears to have promising antitumor activity in previously treated HCC patients. The drug will be further developed in this setting.

6618 POSTER

Results of a multi-center phase II study of imatinib and fluorourcail/leucovorin (FU/LV) in patients with unresectable or metastatic gallbladder or biliary tract cancer

K. Schuette[1], M. Moehler[2], E. Kettner[3], S. Hegewisch-Becker[4], E. Goekkurt[1], S. Al-Batran[5], C. Steffens[6], G. Ehninger[1], J. Stoehlmacher[1]. *[1]Universitätsklinikum Carl Gustav Carus, Medizinische Klinik I, Dresden, Germany; [2]Universitätsklinikum Mainz, Medizinische Klinik, Mainz, Germany; [3]Klinikum Magdeburg, Hämatologie/Onkologie, Magdeburg, Germany; [4]Onkologische Schwerpunkt-Praxis Hamburg, Onkologie, Hamburg, Germany; [5]Krankenhaus Nordwest, Medizinische Klinik II, Frankfurt, Germany; [6]Onkologische Praxisgemeinschaft, Onkologie, Stade, Germany*

Background: There are no standard chemotherapeutic regimens for incurable biliary adenocarcinomas. Monotherapies with gemcitabine or FU/LV achieve occasional responses and a median overall survival of about 6 months. By blocking PDGFR a decreased intrastromal pressure may increase therapy effects of chemotherapy. The combination of imatinib and FU/LV has been shown to be safe and feasible in a previous Phase I trial. This multicenter phase II trial was designed to investigate the disease control rate (DCR) of FU/LV and imatinib.
Methods: Eligibility criteria included unresectable or metastatic measurable biliary tract cancer (BTC)/gallbladder cancer (GBC), performance status ⩽2, adequate organ function and no clinically significant cardiovascular disease. Enrollment of planned 44 chemonaive patients (pts.) was completed. Pts. received LV 200 mg/m^2 followed by FU 2000 mg/m^2 as a 24-hour infusion on days 1 and 2 combined with 600 mg imatinib on days −4 to 4 (8 days). Cycles were repeated every 2 weeks up to 12 cycles. Radiological assessments were performed every 4 cycles.
Results: 44 pts (19 GBC; 25 BTC) were enrolled in this phase II study between 05/07−04/09. Median age was 62 years (range 33−77), male/female = 25/19, ECOG 0/1/2=13/26/5. 38 pts. showed metastatic disease at baseline. Treatment was well tolerated. Treatment related grade 3/4 toxicities included (number of pts): diarrhea (2), edema (1), neutropenia (2), nausea (2), transient SGPT elevation (4). 29 pts. were available for response evaluation at time of analysis. The DCR of these 29 pts. available for response assessment was 55.1% (16 pts) (1 CR, 2 PR, 13 SD of at least 4 cycles). 13 pts. (44.9%) showed progressive disease (PD) per RECIST criteria. 3 pts. had disease stabilization after 12 cycles and continue on treatment. Of pts. not available for analysis five are still on treatment before first evaluation of tumor response; pts. were excluded from analysis due to screening failure (3), lost to follow-up (2) withdraw of consent (1), toxicity (2), other (2).
Conclusions: Our data suggest that the combination of FU/LV and imatinib can be safely administrated in pts. with GBC/BTC. Evidence of antitumor activity was seen in majority of patients. Some pts. achieved long term stabilization of the disease.

6619 POSTER

Early skin toxicity as a predictive factor for tumour control in HCC patients treated with Sorafenib

O. Venditti[1]. *[1]University Campus Bio-Medico, Medical Oncology, Rome, Italy*

Introduction: Sorafenib (Nexavar®), an oral multikinase inhibitor that targets Raf kinase and receptor tyrosine kinases, has recently proved to increase median survival and time to progression in patients with advanced HCC. Cutaneous side effects represent one of the most common sorafenib-related toxicities. This study was conducted to assess the link between the antitumour efficacy of sorafenib and its early cutaneous side-effects considering that a confirm of this connection could lead to the identification of an important predictive factor for tumour control in patients with advanced HCC.
Materials and Methods: we retrospectively analysed the incidence of the skin toxicity (rash and hand-foot skin reaction) as definied by NCI-CTCAE criteria v 3.0 (grading criteria) during the first month of treatment with sorafenib. All patients received 800 mg daily of sorafenib and treatment continued until the occurrence of radiologic progression, defined by RECIST criteria, or the occurrence of either unacceptable adverse events or death. We compared tumour control rate (partial response + stable disease) and progression free survival.
Results: sixty-five HCC patients treated with Sorafenib were included in this analysis: forty-seven of them (73.3%) received sorafenib after failure of some local treatment, while 18 (27.7%) received it as first-line treatment. In 48 (73.8%) patients HCC disease was confined in the liver and in 17 (26.2%) the tumor was diffuse to other organs. All patients were classified as Child A and B. During Sorafenib treatment 29 patients developed at least G1 skin toxicity (13 patients rash and 16 HFS). In patients who developed skin toxicity the tumor control rate was 48.3% vs 19.4% in patients without cutaneous side-effects (P = 0.028). Median PFS was 8.6 months (95% C.I.: 6.5−11.6) in the group of patients with skin toxicity vs 4.3 months (95% C.I.: 2.1−6.1) in patients who did not developed skin toxicity (P = 0.002). This difference was statistically significant also in multivariate analysis.
Conclusions: the present results suggest that the skin toxicity should be closely monitored in HCC patients treated with sorafenib also in relation with its potential role as predictive factor of efficacy.

6620 POSTER

Pegylated liposomal doxorubicin (PLD) and gemcitabine (G) in the treatment of advanced hepatocellular carcinoma (HCC)

D. Pastorelli[1], F. Zustovich[1], G. Lombardi[1], S. Zovato[1], M. Farina[1], L. Furini[1], G. Faggioni[1], M.O. Nicoletto[1], R. Ceravolo[1]. *[1]Istituto Oncologico Veneto IOV-IRCCS, Oncologia Medica 1, Padova, Italy*

Background: Despite Sorafenib represents the new standard therapy for advanced HCC the patient survival remains still poor. Single-agent

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

J. Raoul[1], A.L. Cheng[2], Y.K. Kang[3], C.J. Tsao[4], J. Zou[5], A. Nadel[6], K. Burock[7], D. Voliotis[6], J.M. Llovet[8], J. Bruix[8]. *[1]Centre Eugène Marquis, Rennes, France; [2]National Taiwan University Hospital, Taipei, Taiwan; [3]ASAN Medical Center Songpa-gu, Seoul, South Korea; [4], Chi Mei Medical Center Liou Ying Campus, Tainan, Taiwan; [5]Bayer Schering Pharma, Shanghai, China; [6]Bayer HealthCare Pharmaceuticals, Montville, USA; [7]Bayer Schering Pharma, Wuppertal, Germany; [8]Barcelona Clinic Liver Cancer (BCLC) Group Liver Unit CIBERehd IDIBAPS Hospital Clinic Barcelona, Barcelona, Spain*

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

J.C. Meneu-Diaz[1], S. Jimenez-Galanes[1], A. Moreno-Elola[1], Y. Fundora-Suarez[1], B. Perez Saborido[1], M. Abradelo Usera[1], V. Barra-Valencia[1], A. Gimeno[1], J. LLenas[1], E. Moreno-Gonzalez[1]. *[1]University Hospital 12 de Octubre, Surgery, Madrid, Spain*

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

S. Iwasa[1], C. Morizane[1], T. Okusaka[1], H. Ueno[1], M. Ikeda[2], S. Kondo[1], Y. Kojima[2], A. Hagihara[1], N. Hiraoka[3]. *[1]National Cancer Center Hospital, Hepatobiliary and Pancreatic Oncology Division, Tokyo, Japan; [2]National Cancer Center Hospital East, Hepatobiliary and Pancreatic Oncology Division, Chiba, Japan; [3]National Cancer Center Hospital, Clinical Laboratory Division, Tokyo, Japan*

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.