6515 POSTER DISCUSSION

Continuous sunitinib treatment in patients with unresectable hepatocellular carcinoma (HCC): A multicenter phase II trial (SAKK 77/06 and SASL 23)

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Background: Sunitinib (SU) is a multitargeted tyrosine kinase inhibitor with antitumor and antiangiogenetic activity. Evidence for clinical activity in HCC was reported in 2 phase II trials [Zhu et al and Faivre et al, ASCO 2007] using either a 37.5 or a 50 mg daily dose in a 4 weeks on, 2 weeks off regimen. The objective of this trial was to demonstrate antitumor activity of continuous SU treatment in patients (pts) with HCC.
Methods: Key eligibility criteria included unresectable or metastatic HCC, no prior systemic anticancer treatment, measurable disease and Child-Pugh A or B liver dysfunction. Pts received 37.5 mg SU daily until progression or unacceptable toxicity. The primary endpoint was progression free survival at 12 weeks (PFS12) defined as 'success' if the patient was alive and without tumor progression assessed by 12 weeks ($\pm$7 days) after registration. A PFS12 of $\leqslant$20% was considered uninteresting and promising if $\geqslant$40%. Using the Simon-two minimax stage design with 90% power and 5% significance the sample size was 45 pts. Secondary endpoints included safety assessments, measurement of serum cobalamin levels and tumor density.
Results: From September 2007 to August 2008 45 pts, mostly male (87%), were enrolled in 10 centers. Median age was 63 years, 89% had Child-Pugh A and 47% had distant metastases. Median largest lesion diameter was 84 mm (range: 18–280) and 18% had prior TACE. Reasons for stopping therapy were: PD 60%, symptomatic deterioration 16%, toxicity 11%, death 2% (due to tumor), and other reasons 4%; 7% remain on therapy. PFS12 was rated as success in 15 pts (33%) (95% CI: 20%, 49%) and failure in 27 (60%); 3 were not evaluable (due to refusal). Over the whole trial period 1 CR and 40% SD as best response were achieved. Median PFS, duration of disease stabilization, TTP and OS were 2.8, 3.2, 2.8 and 9.3 months, respectively. Grade 3 and 4 adverse events were infrequent and all deaths due to the tumor.
Conclusions: Continuous SU treatment with 37.5 mg/d daily is feasible and demonstrates moderate activity in pts with advanced HCC and mild to moderately impaired liver dysfunction. Under this trial design the therapy is considered promising (>13 PFS12 successes).

6516 POSTER DISCUSSION

A scoring system in predicting the risk of hepatocellular carcinoma in chronic hepatitis B carrier

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Background: The risk of hepatocellular carcinoma (HCC) is variable among hepatitis B viral (HBV) carriers. Universal surveillance is costly thus it is important to identify the high risk population. We have reported a prospective intensive surveillance study in 1018 HBV carriers (Mok TS et al. J Clin. Oncol. 05). The aim of current study is to develop a scoring system from this prospective cohort that predicts the risk of HCC according to simple clinical parameters.
Materials and Methods: HBV carriers were recruited at the Prince of Wales Hospital between Oct 1997 and Nov 2000. We updated the database in Dec 2008 and performed univariate and multivariate analyses on clinical factors (gender, age, ascites, cirrhosis, albumin, bilirubin, ALT, AFP, HBV DNA, antiviral treatment). A scoring system is developed according to the top independent predictive factors. Scoring system is validated in a separate non-overlapping prospective cohort (Chan HL et al. Hepatology 00).
Results: Data of 1005 HBV carriers was updated in Dec 2008 (13 excluded because HBV DNA results were unavailable). After median follow-up of 9.95 years, we confirmed diagnosis of 105 HCC by histology. By multivariate analysis, 5 variables including age >50 years, albumin $\leqslant$35 g/l, bilirubin >18 μmol/l, high HBV DNA ($\leqslant$4, 4−6, >6 log) and sonographic evidence of cirrhosis were independently predictive of HCC. We developed the scoring from these factors (Table 1) by applying an integral weight to each factor. The rate of HCC development for low risk (CU score <0.0001). The validation works in separate prospective cohort are ongoing and will be available at the meeting.
Conclusions: We have successfully stratified the risk of HCC among HBV carriers by a simple scoring system. Surveillance may not be indicated for the low risk population while more intensive surveillance is warranted for the high risk group.

Table 1

Variable	Score
Albumin (g/l)	
$\leqslant$35	20
>35	0
Cirrhosis	
Yes	15
No	0
Log HBV DNA	
$\leqslant$4	0
4−6	1
>6	4
Age (year)	
>50	3
$\leqslant$50	0
Bilirubin (μmol/l)	
>18	1
$\leqslant$18	0
CU Score (Total score)	
Low risk	<4
Intermediate risk	4−<20
High risk	$\geqslant$20

6517 POSTER DISCUSSION

International phase 2 trial of ABT-869 in patients with advanced hepatocellular carcinoma (HCC)

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Background: ABT-869 is a novel orally active, potent and selective inhibitor of the VEGF and PDGF platelet derived growth factor families of receptor tyrosine kinases, designed to inhibit angiogenesis, tumor growth, and metastasis.
Material and Methods: This was an open-label, multicenter trial of oral ABT-869 at 0.25 mg/kg QD in Child-Pugh A (C-PA) or QOD in Child-Pugh B (C-PB) patients (pts) until progressive disease (PD) or intolerable toxicity. Key eligibility criteria included unresectable or metastatic HCC; up to one prior line of systemic treatment; and at least one measurable lesion by computed tomography (CT) scan. Primary endpoint was the progression free (PF) rate at 16 weeks. Secondary endpoints included objective response rate (ORR), time to progression (TTP), progression free survival (PFS) and overall survival (OS). All efficacy results are based on radiographic assessment by the central imaging center and clinical assessment by the investigator. Trial abbreviation: *Phase 2 trial of ABT-869 in HCC*. Trial registry number: NCT00517920. Trial status: ongoing; not recruiting; sponsored by Abbott Laboratories. ABT-869 is being developed in collaboration with Genentech.
Results: Of the 44 pts enrolled from 09/07 to 08/08, 84% received no prior systemic therapy. Median age was 62 y (range 20−81). The most common AEs were fatigue (57%), diarrhea (43%), hypertension (HT) and rash (39% each), and oedema peripheral (25%). The most common AEs $\geqslant$Grade 3 were HT (16%) and fatigue (14%). 61% of pts had dose interruptions due to AEs and 30% of pts required dose reductions. The most common reasons for dose interruption included HT (16%), proteinuria (9%), and skin reaction