(9%), which were reversible. 10 pts (all CP-A) remained on study at the time of the analysis. 21 pts had discontinued due to PD (clinical, radiographic or AE related to PD), 9 due to AEs not related to PD, and 4 for other reasons. There was one death possibly related to ABT-869 (intracranial hemorrhage, Day 111, CP-B).

	Point estimate [95% CI]		
	CP-A N = 38	CP-B N = 6	All N = 44
PF rate at 16 weeks, %	34.2 [19.6, 51.4]	16.7 [0.4, 64.1]	31.8 [18.6, 47.6]
ORR, %	7.9 [1.7, 21.4]	0	6.8 [1.4, 18.7]
Estimated median TTP, mo	5.4 [3.6, 14.1]	3.7 [0.7, NR]	3.7 [3.6, 7.3]
Estimated median PFS, mo	5.4 [3.6, 14.1]	1.3 [0.7, 3.7]	3.7 [2.0, 5.5]
Estimated median OS, mo	9.7 [8.7, NR]	2.5 [1.1, 4.5]	9.3 [6.0, 11.0]

ORR per RECIST; NR = not reached.

Conclusions ABT-869 is clinically active in advanced HCC, with an acceptable safety profile. Further study of ABT-869 in this setting is warranted.

6518 POSTER DISCUSSION

Evaluation of vandetanib in patients with inoperable hepatocellular carcinoma (HCC): a randomized, double-blind, parallel group, multicentre, Phase II study

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Background: Vandetanib is a once-daily oral anticancer agent that targets VEGFR, EGFR and RET signalling. The efficacy and safety of vandetanib was investigated in Taiwanese patients with inoperable HCC (study codes D4200C00072; NCT00508001).
Materials and Methods: Eligible patients with Child–Pugh class A, inoperable HCC were randomized 1:1:1 to receive vandetanib 300 mg/day + best supportive care (BSC), vandetanib 100 mg/day + BSC or placebo + BSC until disease progression. Patients receiving vandetanib 100 mg or placebo were eligible to receive open-label vandetanib 300 mg after progression. The primary objective was to evaluate tumour stabilization rate (complete response + partial response + stable disease $\geqslant$4 months). Secondary assessments included progression-free survival (PFS), overall survival (OS) and safety.
Results: Between July 07–Nov 08, 67 patients (55 male/12 female; mean age, 58 years) were randomized to vandetanib 300 mg (n = 19), vandetanib 100 mg (n = 25) or placebo (n = 23). At data cut-off, 59 patients had progressed, 40 had died and 28 had entered treatment with vandetanib 300 mg after progression. In both vandetanib arms, the primary endpoint of tumour stabilization rate was not significantly different from placebo; however, vandetanib treatment showed positive trends for PFS and OS, including significant prolongation of OS versus placebo in patients randomized to vandetanib 100 mg (see Table).

Table. Efficacy summary (intent-to-treat population)

	Vandetanib		Placebo
Efficacy assessment	300 mg N = 19	100 mg N = 25	N = 23
Tumour stabilization rate	5.3%	8.0%	4.3%
Odds ratio vs placebo	1.22	1.98	–
P value	1.00	1.00	–
Median PFS (weeks)	7.0	7.1	4.0
PFS hazard ratio vs placebo	0.557	0.643	–
P value	0.0898	0.158	–
Median OS (months)	6.0	5.6	3.9
OS hazard ratio vs placebo	0.481	0.447	–
P value	0.077	0.037	–

Treatment was generally well tolerated, with a median duration of 5.6 weeks (vandetanib 300 mg), 6.1 weeks (vandetanib 100 mg) and 4.3 weeks (placebo). The most common adverse events were diarrhoea and rash, which occurred more frequently in the vandetanib 300 mg arm (42% and 47%, respectively) compared with vandetanib 100 mg (28% and 20%) or placebo (30% and 26%). Four adverse events led to treatment discontinuation: hepatic failure (vandetanib 300 mg), and diarrhoea, hyperbilirubinaemia and upper gastrointestinal haemorrhage (all placebo).
Conclusions: In this small study of Taiwanese patients with advanced inoperable HCC, the primary endpoint of improved tumour stabilization rate was not met with vandetanib (100 or 300 mg) versus placebo. However, the PFS and OS results suggest vandetanib has clinical activity in this patient population that may warrant further investigation. The safety profile was consistent with previous studies of vandetanib in patients with advanced cancer.

6519 POSTER DISCUSSION

Efficacy and safety of sorafenib in patients with advanced hepatocellular carcinoma (HCC): collective results from the phase III sorafenib HCC assessment randomized protocol (SHARP) and Asia-Pacific (AP) trials

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Background: The frequency of viral etiologies of hepatocellular carcinoma (HCC) varies between geographic populations. The hepatitis virus B predominates in many Asian populations, while hepatitis virus C underlies most HCCs in Western countries. Whether these different etiologies result in tumors that respond differently to treatment is unknown. Here, we compared results of the SHARP and AP trials to evaluate the effectiveness of sorafenib in patients worldwide with advanced HCC. SHARP enrolled patients from Europe, North/South America, and Australia; the AP trial enrolled patients from the AP region.
Methods: Eligibility criteria were similar for the two trials. Patients had advanced HCC, Child-Pugh A, ECOG PS 0−2, and no prior systemic therapy for HCC. Patients were randomized to sorafenib 400 mg BID or placebo, at a 1:1 (SHARP) or 2:1 (AP) ratio. Endpoints included overall survival (OS), time to progression (TTP), and safety.
Results: Efficacy and safety results are summarized in the table below. AP patients had more advanced disease (eg, more extrahepatic spread, poorer ECOG PS) than SHARP patients at baseline. OS and TTP hazard ratios were similar between SHARP/AP studies, despite more advanced disease in AP patients. The incidence of grade 3/4 adverse events (AEs) was similar in all sorafenib populations and included hand-foot skin reaction (HFSR), diarrhea, fatigue, and hypertension. When comparing all grades of AEs, HFSR was more common in the AP population and diarrhea in the SHARP trial. The treatment discontinuation rates were similar in both trials.
Conclusions: Sorafenib was effective and safe for the treatment of advanced HCC regardless of etiology, despite a more evolved HCC stage in Asia.

	SHARP Study		AP Study	
Endpoint	Sorafenib/Placebo median (months) (N = 299)/(N = 303)	Hazard Ratio (95% CI)	Sorafenib/Placebo median (months) (N = 150)/(N = 76)	Hazard Ratio (95% CI)
Overall survival	10.7/7.9	0.69 (0.55−0.87)	6.5/4.2	0.68 (0.50−0.93)
Time to progression	5.5/2.8	0.58 (0.45−0.74)	2.8/1.4	0.57 (0.42−0.79)

Incidence of drug-related AEs in Sorafenib and Placebo groups

Drug-related AE	Incidence, Sorafenib/Placebo (%)			
	SHARP Study		AP Study	
	All Grades (N = 297)/(N = 302)	Grade 3/4 (N = 297)/(N = 302)	All Grades (N = 149)/(N = 75)	Grade 3/4 (N = 149)/(N = 75)
HFSR	21/3	8/<1	45/3	11/0
Diarrhea	39/11	8/2	26/5	6/0
Fatigue	22/16	4/4	20/8	3/1
Hypertension	5/2	2/1	19/1	2/0