Patients and Methods: Patients with locally advanced or metastatic RCC, who may have received radiation therapy and/or one biologic response modifier regimen, were enrolled. Patients received 8-week cycles of continuous oral sorafenib 400 mg bid with subcutaneous IFN alpha-2b 10 MIU tiw. Patients continued to receive treatment until disease progression, unacceptable toxicity or death. To resolve toxicities, a 2-week treatment break between cycles was permitted.
Results: Fourteen of a planned 40 patients were enrolled. Patients' characteristics were: median age 58 years (range 33–81); ECOG 0:1, 86%:14%; prior therapy, 64%; prior IL-2, 50%; prior nephrectomy, 93%; ⩾2 metastatic sites, 50%; clear-cell histology, 71%. Of the eight patients evaluable for tumor response after Cycle 1, three patients had a partial response, one patient had a minor response and three patients had stable disease. Three of the responders had failed prior IL-2. Five patients experienced dose-modifying toxicities of grade 2 fatigue (n = 2), diarrhea or hypoalbuminaemia (n = 1 each), grade 3 rash (n = 2) or abnormal AST/ALT (n = 1), and grade 4 neutropenia (n = 1). Frequent toxicities included grade 1/2 fatigue/depression (n = 9), rash (n = 5), diarrhea (n = 3), hypophosphataemia and nausea/vomiting (n = 2 each). Grade 3/4 events included rash (n = 2), elevated lipase, leukopenia, neutropenia and hypophosphataemia (n = 1 each).
Conclusions: Oral sorafenib 400 mg bid plus IFN alpha 2b 10 MIU tiw shows preliminary evidence of anti-tumor activity both in untreated patients and in IL-2 failures, and appears to be safe and well tolerated in patients with metastatic RCC. Further data, including the effects on signaling in tumors, will be updated at the meeting.

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Bevacizumab, erlotinib, and imatinib in the treatment of patients (pts) with advanced renal cell carcinoma (RCC): Update of a Minnie Pearl Cancer Research Network phase I/II trial

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Background: The overexpression of vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and platelet-derived growth factor (PDGF) in renal cell cancer (RCC) provides rationale for combining novel biologic agents which inhibit these receptors. In a prior multicenter phase II trial, combined VEGF/EGF receptor inhibition with bevacizumab and erlotinib was an active and safe regimen for pts with metastatic RCC. In this phase I/II trial, we added imatinib, which targets PDGF expression, to bevacizumab/erlotinib.
Methods: Eligibility: metastatic clear cell RCC, 0–2 previous systemic regimens, ECOG PS 0–1, no previous anti-angiogenesis or EGF receptor inhibitor therapy, no active CNS metastases, adequate organ function, no history of thromboembolic disease, informed consent. All pts received bevacizumab 10 mg/kg IV q 2 weeks, and erlotinib 150 mg po daily. In the phase I portion of the trial, imatinib levels were escalated: 300 mg qd (cohort 1), 400 mg qd (cohort 2), and 600 mg qd (cohort 3). Pts were evaluated for response after 8 weeks using RECIST criteria; treatment continued until tumor progression.
Results: In the phase I portion of the trial, imatinib 400 mg qd was identified as the maximum tolerated dose. At this dose level, 2 of 10 patients had reversible dose-limiting toxicity (diarrhea). Between 7/04 and 3/05, 91 pts were treated. This report contains preliminary results on the first 48 patients entered (44 evaluable). Pt characteristics included: median age 63 years; male/female, 37/11; ECOG 0/1, 14/34; 34 pts (71%) were previously untreated; the remainder had received IL-2 and/or interferon. Four of 44 evaluable pts (9%) had objective responses (all PR). Twenty-seven pts (61%) had stable disease; however, 6 of these pts (14% of total) had minor objective responses (10–30% decrease by RECIST criteria). Progression-free and overall survivals at 9 months are 66% and 70%, respectively. The median duration of follow-up is 5 months (range 3–10 months). Grade 3/4 toxicity: diarrhea 29%; rash 27%; nausea/vomiting 13%; hypertension 2%; bleeding 2%; proteinuria 2%; fatigue 6%.
Conclusions: The combination of bevacizumab, erlotinib, and imatinib is active in pts with metastatic RCC. Although tolerable for most patients, imatinib appears to increase the frequency and severity of diarrhea, rash, and fatigue. Further follow-up of the entire 91 patients on this trial is necessary prior to making final conclusions regarding this combination regimen. Updated results on the entire group of 91 pts will be presented.

797 ORAL

Sunitinib malate (SU11248) shows antitumour activity in patients with metastatic renal cell carcinoma: updated results from phase II trials

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Background: In clear cell renal cell carcinoma (RCC), loss of VHL gene function results in up-regulated expression of VEGF and PDGF. Sunitinib malate is an oral multitargeted tyrosine kinase inhibitor of VEGFR and PDGFR and has demonstrated both antiangiogenic and antitumour activities in phase I trials in RCC and other tumour types. Therefore, we evaluated the antitumour activity and safety of sunitinib in patients (pts) with metastatic RCC in two independent single-arm, phase II trials.
Patients and methods: Eligibility for both trials included measurable disease, failure of one prior cytokine therapy, ECOG PS of 0/1, and adequate organ function. Pts received sunitinib 50 mg q.d. orally for 4 weeks, followed by 2 weeks off treatment to comprise a cyclical 6-week regimen. Best response was assessed using RECIST.
Results: Trial 1 enrolled 63 pts (Jan 03 – Jul 03) and Trial 2 (ongoing) enrolled 106 pts (Feb 04 – Nov 04). Best responses for evaluable pts are shown in Table 1 and are presented as of Apr 05.

Table 1. Best response to sunitinib in RCC pts.

	Objective response N (%)	CR N (%)	PR N (%)	SD ⩾3 months N (%)	PD or SD <3 months N (%)	Not evaluable N (%)
Trial 1 (N = 63)	25 (40)	0 (0)	25 (40)	18 (29)	16 (25)	4 (6)
Trial 2 (N = 106)*	42 (40)	1 (1)	41 (39)	24 (23)	33 (31)	7 (7)

*Study ongoing

Of 25 pts who achieved a PR in Trial 1, the median duration of response is 12.5 months (range 2–19+). The median TTP is 8.7 months and median survival is 16.4 months. Currently, 8 PRs are progression-free at 21+ to 24+ months (from start of therapy), including 6 pts remaining on therapy and 2 rendered disease-free by surgery. In Trial 2, of 24 pts with best response of SD, 5 had tumour reduction of 30% and await confirmation of response status. Overall, the majority of treatment-related adverse events and haematological abnormalities were grade 1 and 2, and included (Trial 1, Trial 2): fatigue (38%, 22%), diarrhoea (24%, 16%), stomatitis (19%, 14%), neutropenia (45%, 39%), anaemia (37%, 25%), and thrombocytopenia (18%, 19%).
Conclusions: Two consecutively conducted phase II trials demonstrate that sunitinib has substantial antitumour activity in pts with metastatic RCC. The objective response achieved in Trial 1 (40%) was confirmed independently in Trial 2 (40%). Sunitinib has manageable adverse events, with responding pts receiving treatment for over 2 years. Further studies to explore sunitinib as first-line therapy are underway.

798 ORAL

A prospective study of 18FDG PET in the prediction of relapse in patients with high risk clinical stage I non-seminomatous germ cell cancer (MRC study TE22)

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Background: Optimum management of patients with clinical stage I (CS1) non-seminomatous germ cell tumours (NSGCT) has been debated; options include adjuvant chemotherapy, retroperitoneal lymph node dissections (+/− adjuvant chemotherapy) and initial surveillance with treatment at relapse. Each approach achieves similarly high cure rates (>98%).