completed the 1st treatment course have received additional courses; none have discontinued therapy due to progressive disease.
**Conclusions:** Outpatient therapy with rIL-21 plus sorafenib is well tolerated with appropriate dose modification and associated with anti-tumor activity as a 2nd or 3rd-line therapy for mRCC. Updated results from all available subjects in Phase 2, including 6 months of follow-up for the first 15 subjects, will be available at the meeting.

**205** POSTER

**A phase II study of oral enzastaurin HCl in patients with metastatic colorectal cancer**

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**Background:** About 50% of all colorectal cancer (CRC) patients (pts) ultimately die of metastatic disease signifying a need for improved treatment. Enzastaurin, a protein kinase C-β/AKT inhibitor with antiangiogenic and proapoptotic properties, has shown activity in hematological and solid tumors. We evaluated enzastaurin monotherapy using a Phase 2 Window study in chemonaive pts with asymptomatic metastatic CRC (mCRC) for whom standard chemotherapy could be safely delayed. The main objective of this single-arm, open-label study was to estimate the 6-month progression-free survival (PFS); secondary objectives included evaluation of safety and efficacy, time-to-event measures, and carcinoembryonic antigen (CEA) levels.
**Materials and Methods:** Patients with asymptomatic mCRC with Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 with at least one measurable lesion received a 400 mg TID loading dose of enzastaurin on Day 1 of Cycle 1, followed by 500 mg once daily for the remaining cycle (1 cycle = 28 days), and all subsequent cycles. Patients were considered eligible only if they were not candidates for chemotherapy-induced tumor reduction that could potentially lead to total tumor resection. Plasma samples for pharmacokinetic characterization were collected on Day 2, Cycle 1 (day after loading dose); Day 1, Cycle 2; and Day 1, Cycle 3 (both steady-state).
**Results:** A total of 28 pts (16 male, 12 female; median age 69 yrs) enrolled and received treatment. Six (21%, 95% CI = 13−44%) pts reached a 6 month PFS. No pt had a clinical response, 12 (43%) achieved stable disease. Overall survival was censored at 82%. The survival rate at 20 months = 77% (CI 47%-92%) and median PFS was 2 months (95% CI = 1.8–4.5 months). Correlation between CEA level changes and enzastaurin activity was not apparent. Four of 28 pts received the planned 6 cycles of therapy. Of the 2 discontinuations, one (cerebral hemorrhage leading to death) was possibly related to study drug. There were 4 dose omissions but no dose reductions. Eight pts had Grade (Gr) 3 toxicities and 1 pt had a Gr 4 upper respiratory infection. The Gr 3 toxicities included nausea, transaminase elevation (possibly related to study drug), edema, etc, but no prevalence of any specific toxicity was evident. Alterations in QTc intervals observed on electrocardiogram assessments were not deemed medically significant even when conducted at Cmax level. Slit-lamp exams did not indicate cateractogenesis or changes in existing cataracts with enzastaurin treatment. Pharmacokinetics of enzastaurin and its active metabolite in mCRC pts were comparable to those seen in previous studies in other tumor types.
**Conclusions:** Enzastaurin is well tolerated but exhibits modest activity as monotherapy in chemonaive pts with mCRC. Further studies of enzastaurin in combination with other agents in mCRC are warranted.

**206** POSTER

**Phase II study of sunitinib in patients (pts) with progressive metastatic adenoid cystic carcinoma (ACC)**

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**Background:** A high level of c-kit expression, usually of wild-type, has been identified in >90% of ACC. However, imatinib has been found to be inactive in that population likely because its activity is dependent on specific c-kit mutations (Hotte et al, J Clin Oncol 2005). VEGF overexpression has been correlated with worse clinical outcome in ACC (Zhang et al, Clin Cancer Res 2005). Sunitinib, which inhibits multiple receptor tyrosine kinases including VEGFR and unmutated c-kit, is of interest for evaluation in ACC.
**Methods:** This is a two-stage, single-arm phase II clinical trial of sunitinib in adult pts with unresectable or metastatic ACC measurable by RECIST criteria, progressive disease is not mandatory at study entry. All patients were treated with a starting dose of sunitinib 37.5 mg PO on a daily and continuous schedule, in 4-week cycles. The primary endpoint is objective response rate, assessed radiologically every 8 wks. One or more objective responses must be observed out of 12 pts in the first stage for the study to enrol to a total of 37 pts.
**Results:** Since February 2007, 12 pts, including 8 males, with a median age of 61 (range, 50−70) were entered onto stage 1. Nine pts had no prior systemic treatments and 11 had prior radiation. Pts had a median of 5 target sites (range, 2−9) and lung lesions were most common. A total of 56 cycles and a median of 5 cycles (range, 2−8) have been administered. All pts but one had a best response of SD and 2 pts remain on study. No PR observed; PFS was nine months (mo) (95%CI 7.3 – NR) and 6-month progression free rate was 91%. Median time to failure was 7.3 mo (95%CI 6.6 mo – NR). This compares favourably to other phase 2 trials conducted by our group (Table). Four pts came off study because of toxicity. The most frequent adverse events (AE) of all grades and at least possibly related to sunitinib were (# of pts): fatigue (9), lymphopenia (9), mucositis (8), leucopenia (7), dyspepsia (7), hypophosphatemia (7), diarrhea (6), neutropenia (6), hand foot syndrome (6). Grade 3 AE of possible attribution were infrequently encountered (# of pts) and most common were: lymphopenia (4), fatigue (4) and neutropenia (3).
**Conclusions:** Sunitinb is associated with the expected toxicities but is reasonably well tolerated and may favourably affect rate of progression of disease. Decision regarding proceeding to second stage is pending.

Table 1

| | lapatinib (mo) | imatinib (mo) | sunitinib (mo) |
|---|---|---|---|
| Median TTP | 3.5 (31-NA) | 2.3 (1.8-NA) | 9 (7.3-NA) |
| 3-mo PFS | 70% (53−93%) | 37% (19−74%) | – |
| 6-mo PFS | 35% (19−64%) | 20% (6−62%) | 91% (75–100%) |

**207** POSTER

**Phase II study of gefitinib in combination with cisplatin and concurrent radiotherapy in patients with stage III/IV squamous cell head and neck cancer and to analyse the effect of gefitinib on tumour gene expression**

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**Background:** Gefitinib has shown modest activity in squamous cell head and neck cancer (SCHNC) and is synergistic with radiation and cisplatin in exerting anti-tumour effects. This study aims to determine the feasibility and toxicity of adding gefitinib to cisplatin and concurrent radiotherapy in patients with locally advanced SCHNC.
**Methods:** Patients with accessible primary tumour site for repeat biopsies and who have stage III/IV unresectable SCHNC or who were deemed unsuitable for curative resection were eligible. Baseline biopsy of the tumour at the primary site was done and the patient was started on gefitinib at 500 mg/day as induction for 3 weeks. Two weeks after the start of gefitinib, a second tumour biopsy was done. A repeat CT/MR of the head/neck was done after the induction phase for response evaluation. Radiotherapy of 70 Gy in standard fractionation was started after induction phase with cisplatin at 80 mg/m$^2$ given on weeks 1, 4 and 7 of the radiation concurrently. Gefitinib was maintained at 500 mg/day during the radiotherapy phase and continued for 4 months as consolidation upon completion of radiotherapy. A repeat CT/MR was done 8 weeks after completion of radiation for evaluation and 3−4 monthly thereafter for the first 2 years. The paired tumour samples were analysed for changes in gene expression after gefitinib using the Affymetrix Gene Chip Human Genome U133 set.
**Results:** 31 patients were recruited; one patient declined further treatment after 1 week of induction gefitinib. Patient characteristics are as follows: median age 55 yrs (44−77), male 77%, eversmoker 68%. Tumour characteristics: oral cavity 36%, oropharynx 45%, others 19%; T1−2 19%, T3−4 81%, N0−1 32%, N2−3 68%. Three pts responded during induction phase (10%) with 2 complete responses (CR); at the first evaluation after completion of chemoradiotherapy, 74% had a major response (PR/CR). The 2-yr progression-free (PFS) and overall survival rate (OS) was 45%