and 61% respectively. The treatment schedule was generally well tolerated with oropharyngeal mucositis as the main toxicity: 65% grade 2 and 29% grade 3. Grade 3 neutropenia occurred in 3 patients (10%). One patient died of acute myocardial infarction during the treatment. Relative dose intensities of gefitinib was good at a median of 95% (49–100); 13 patients (42%) completed the intended gefitinib dose. Eleven patients were not able to receive the 3rd cycle of cisplatin due mainly to mucositis. There were 14 paired tumour samples suitable for gene expression analysis. Analysis is still ongoing and will be presented at the meeting.
Conclusion: The combination of gefitinib and cisplatin with concurrent radiotherapy is feasible and well accepted by patients with stage III/IV SCHNC with 2-yr PFS and OS which are encouraging.

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A phase II study of sunitinib, an oral multi-targeted tyrosine kinase inhibitor, in patients with unresectable, locally advanced or metastatic cervical carcinoma: IND184

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Background: Sunitinib malate (SU11248) is an oral, multi-targeted tyrosine kinase inhibitor targeting VEGFR, PDGFR, KIT and FLT3. Patients with advanced or metastatic cervix cancer have a poor prognosis and have low response rates to conventional chemotherapy. In preclinical and clinical models VEGFR and c-kit, amongst other receptor tyrosine kinases, have been implicated in the development and progression of cervical cancer.
Methods: The aim of this multi-centre 2-stage design phase II study was to assess the activity of sunitinib in patients (pts) with locally advanced or metastatic cancer of the cervix. Eligibility criteria included: squamous cell, adenosquamous or adenocarcinoma histology, ECOG PFS 0−1. Prior neoadjuvant, adjuvant or concurrent chemoradiation and up to 1 prior line of chemotherapy for metastatic disease were allowed. Primary endpoint was objective response, secondary endpoints included duration of response, time to progression and tolerability. Pts received sunitinib 50 mg/day for 4 wks followed by 2 wks off treatment in 6-wk cycles. Tumor response was assessed by RECIST criteria every cycle. One response out of the first 18 patients had to be observed to proceed to the second stage of accrual.
Results: 19 pts enrolled, 15 with prior chemoradiation, median age 44 (range 28−78) yrs received a total of 55 cycles of treatment (median 2; range 1 to 6). 15 pts have had stable disease and 4 progressive disease: 2 pts remain on treatment. The most common drug related adverse events any grade (% of patients) were diarrhea (74%), fatigue (74%), nausea (58%), hypertension (47%), taste alteration (53%) and hypopigmentation (58%). Grade 3/4 lymphopenia was seen in 8 pts with grade 3/4 anemia in 4. Thyroid stimulating hormone was elevated in 9 pts. 6 pts have developed fistula on study (3 possibly drug related): 5 had received prior chemoradiation and the remaining pt adjuvant radiation alone following surgery. 1 pt died on study (symptomatic progression, hemorrhage/fistula). Three serious unexpected and possibly drug related adverse events have been seen (1 pt with dyspnea and fall in LVEF, 1 pt with pulmonary infiltrates and 1 pt with PV hemorrhage). 7 pts required dose reduction, there were 114 missed doses (58 drug related) in 10 pts.
Conclusions: Sunitinib has insufficient activity in cervix cancer to warrant further investigation. The higher than expected rate of fistula formation in this population is of concern. The study has closed to accrual.

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An open-label, multicenter, phase 1/2 study of AT-101 in combination with docetaxel and prednisone in men with hormone refractory prostate cancer

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Background: Antiapoptotic Bcl-2 family proteins are overexpressed in hormone refractory prostate cancer (HRPC) and contribute to resistance to therapy. The oral, pan-Bcl-2 (Bcl-2, Bcl-XL, Bcl-W, Mcl-1) inhibitor AT-101 is active as a single agent in men with HRPC and in combination with docetaxel in in vitro and in vivo prostate cancer tumor models. In this Phase 1/2 study, men at least 18 years of age with chemotherapy-naive HRPC were treated with docetaxel 75 mg/m^2 q3 weeks, prednisone 5 mg/b.i.d. on days 1−21, and AT-101 at 40 mg/b.i.d. on days 1−3 of each cycle.
Material and Methods: The primary objectives of this study were to assess PSA response (Bubley criteria) and toxicities to treatment (NCI CTCAE v. 3.0). Secondary objectives include time to PSA response, duration of PSA response, time to PSA progression, and objective tumor responses (RECIST).
Results: This analysis includes 20/37 subjects who received >3 months of treatment. Subject characteristics: median age 69.5 (55−84), median baseline PSA was 174 ng/ml with all subjects having a PSA level >20 ng/mL; 40% had a Gleason score of 8−10; 85% progressed following >2 prior hormonal therapies; 75% had bone metastases; 65% had visceral disease; and all subjects treated had evidence of PSA progression at study entry. Preliminary results showed that 70% (14/20) of subjects achieved a partial response (>50% PSA decline), 80% (16/20) had at least a 30% decrease in PSA level, and 5% (1/20) were refractory to therapy based on PSA measurements. PSA response data is presented graphically in the Waterfall plot. The median time to response was 42.5 days. Of the subjects with measurable disease 54% (6/11) had a PR per RECIST. Six subjects are still on therapy and, thus far, 30% (6/20) of subjects have received >10 cycles of therapy. Mature data regarding duration of response and time to progression are not yet available. Safety data was available on 15 subjects. The majority of AEs were Grade 1/2 (60%/29%); 6% were Grade 3 and 2% were Grade 4. The most common AEs experienced included fatigue (9/15), diarrhea (6/15), nausea (5/15), taste alteration (5/15), constipation (4/15), alopecia (4/15), dehydration (3/15), vomiting (3/15), abdominal pain (3/15), hypomagnesemia (3/15), and edema (3/15).
Conclusions: Preliminary data suggests that oral AT-101 when given in combination with docetaxel and prednisone is well tolerated and shows preliminary evidence of efficacy in subjects with HRPC.