**51LBA** LATE BREAKING ABSTRACT

**Completion of a Phase II study of sorafenib for advanced thyroid cancer**

M.S. Brose[1], A.B. Troxel[2], K. Harlacker[3], M. Redlinger[3], A.A. Chalian[4], L.A. Loevner[5], S.J. Mandel[6], P.J. O'Dwyer[7], S.M. Keefe[3]. [1]*Abramson Cancer Center University of Pennsylvania, Otorhinolaryngology: Head and Neck Surgery and Medicine Hematology/Oncology, Philadelphia PA, USA;* [2]*Abramson Cancer Center University of Pennsylvania, Biostatistics and Epidemiology, Philadelphia PA, USA;* [3]*Abramson Cancer Center University of Pennsylvania, Medicine Hematology/Oncology, Philadelphia PA, USA;* [4]*Abramson Cancer Center University of Pennsylvania, Otorhinolaryngology: Head and Neck Surgery, Philadelphia PA, USA;* [5]*Abramson Cancer Center University of Pennsylvania, Radiology, Philadelphia PA, USA;* [6]*Abramson Cancer Center University of Pennsylvania, Medicine Division of Endocrinology, Philadelphia PA, USA*

**Background:** Patients with advanced thyroid cancer have few treatment options and chemotherapy has little clinical benefit. From February 2006 to May 2009 we enrolled 55 patients on an open-label phase II study of sorafenib in patients with metastatic, iodine-refractory thyroid carcinoma.
**Materials and Methods:** Patients were administered sorafenib 400 mg orally BID. Responses were monitored by PET and CT. Primary endpoints were response rate (RR) and progression free survival (PFS) by RECIST criteria and a secondary endpoint was overall survival (OS). *BRAF* and *RAS* mutation status was determined by DNA sequencing. Outcome data was evaluated using the Kaplan–Meier method and log-rank test. Biologic activity in tissue obtained during treatment at response and progression is being explored using quantitative immunohistochemistry (IHC) to pERK, and pAKT and among others, on pretreatment blocks which were available from 47 of the 55 patients.
**Results:** We have completed accrual of the 55 patients planned for enrollment; median time on study is 39 weeks and 27 pts (49%) are male. Of the 23 patients that are off study, 14 developed progressive disease, 7 withdrew for medical reasons that not due to progression of disease, 5 withdrew due to toxicity and 2 withdrew due to non-compliance. Histological subtypes include papillary (PTC): 29 pts (53%); follicular/Hürthle Cell (FTC): 18 pts (33%) for a total of DTC of 47 (85%); medullary: 3 pts (5%), and poorly differentiated/anaplastic: 5 pts (9%). 53/55 patients are evaluable for response at this time. Median PFS was 63 weeks and overall survival was 140 weeks. PFS for patients with DTC was 84 wks and OS has not been reached. Genotyping of *BRAF* revealed a trend toward improved outcome but was not significant. On-treatment tissue at progression demonstrates heterogeneity, with p-ERK and p-AKT suppressed in some areas, but highly expressed in others. Response data on all 55 patients at 4 months post accrual of the last patient will be presented.
**Conclusions:** Sorafenib has significant clinical activity in patients with advanced thyroid cancer with an OS of 140 weeks and an overall PFS of 84 wks for patients with DTC. Our data show that sorafenib warrants further investigation in a large Phase III study for DTC.

**52LBA** LATE BREAKING ABSTRACT

**Final report of NPC-9902 trial on therapeutic gain and late toxicities by concurrent-adjuvant chemotherapy and/or accelerated fractionation for T3−4N0−1M0 nasopharyngeal carcinoma**

A. Lee[1], S.Y. Tung[2], A.T.C. Chan[3], R. Chappell[4], Y.T. Fu[5], T.X. Lu[6], E.H. Tan[7], D.T.T. Chua[8], B. O'Sullivan[9], R. Tung[10]. [1]*Pamela Youde Nethersole Eastern Hospital, Department of Clinical Oncology, Hong Kong, Hong Kong;* [2]*Tuen Mun Hospital, Department of Clinical Oncology, Hong Kong, Hong Kong;* [3]*Prince of Wales Hospital, Department of Clinical Oncology, Hong Kong, Hong Kong;* [4]*University of Wisconsin Medical School, Department of Biostatistics, Madison, USA;* [5]*Queen Elizabeth Hospital, Department of Clinical Oncology, Hong Kong, India;* [6]*Sun Yat Sen University, Cancer Center, Guangzhou, China;* [7]*National Cancer Center, Department of Medical Oncology, Singapore, Singapore;* [8]*Queen Mary Hospital, Department of Clinical Oncology, Hong Kong, Hong Kong;* [9]*Princess Margaret Hospital, Ontario Cancer Institute, Ontario, Canada;* [10]*Hong Kong Cancer Fund, Department of Service, Ontario, Canada*

**Purpose**: To evaluate the therapeutic ratio achieved by adding concurrent-adjuvant chemoradiotherapy (+C) and/or accelerated fractionation (AF) versus radiotherapy alone with conventional fractionation (CF) for locally advanced nasopharyngeal carcinoma (NPC). This is one of the first trials with long term data on late toxicities in addition to survival rates.
**Patients and Methods:** All eligible patients were irradiated with the same RT technique to $\geqslant$66 Gy at 2 Gy/fraction in line with policy of individual participating center. The number of fractions/week was 5 for those randomly assigned to the CF and CF+C arms, and 6 for the AF and AF+C arms. Patients in the CF+C and AF+C arms were given the Intergroup-0099 Regimen of cisplatin 100 mg/m$^2$ every 3 weeks for 3 cycles in concurrence with RT, followed by 3 adjuvant cycle of cisplatin 80 mg/m$^2$ and 5-fluorouracil 1000 mg/m$^2$/day for 96 hours every 4 weeks. All analyses are based on intention-to-treat principle.
**Results:** From March 1999 to April 2004, 189 patients have been accrued; the trial was terminated early because of slow accrual. The median follow-up was 6.2 years. The 4 arms were well-balanced except for higher proportion of male patients in the AF arm (90 vs $\leqslant$78%). The attached Table shows the actuarial tumor control and late toxicity rates, and the independent significance of the two treatment strategy.
**Conclusions:** Long term data suggest that CRT combined with AF could achieve significant improvement in failure-free survival, CRT is an independent factor for improving overall survival, and the increase in late toxicity rates are statistically insignificant.

| | Comparison by log-rank 5-year Actuarial Rate % (p-value) | | | | Multivariate Analyses Hazard Ratio (95% CI) | |
|---|---|---|---|---|---|---|
| | CF | AF | CF+C | AF+C | CRT | AF |
| Loco-regional control | 85 | 75 (0.3) | 81 (0.96) | 9.8 (0.31) | 0.712 (0.336, 1.510) | 0.862 (0.413, 1.796) |
| Distant control | 75 | 74(0.94) | 75(0.95) | 96*(0.05) | 0.770 (0.396, 1.497) | 0.581 (0.300, 1.125) |
| Failure-free rate | 63 | 57(0.44) | 65(0.72) | 88*(0.02) | 0.612b (0.359, 1.044) | 0.707 (0.420, 1.188) |
| Progression-free survival | 62 | 54(0.30) | 60(0.94) | 78(0.09) | 0.696 (0.433, 1.119) | 0.807 (0.507, 1.284) |
| Overall survival | 68 | 66(0.33) | 78(0.59) | 86(0.10) | 0.505* (0.288, 0.885) | 0.990 (0.580, 1.688) |
| Late toxicity (Grade $\geqslant$3) | 20 | 25(0.35) | 34(0.23) | 36(0.32) | 1.268 (0.720, 2.233) | 1.105 (0.636, 1.920) |

*significant on comparison against CF alone.

**53LBA** LATE BREAKING ABSTRACT

**A phase I/IIa study of icotinib hydrochloride (BPI-2009H), an oral epidermal growth factor receptor tyrosine kinases inhibitor, in patients with advanced non-small-cell lung cancer and other solid tumors**

Q. Zhao[1], J. Zhou[1], J. Shentu[2], L. Wu[2], N. Xu[3], F. Tan[4], Y. Wang[4], D. Yang[4]. [1]*The First Affiliated Hospital Zhejiang University, Respiration, Hangzhou, China;* [2]*The First Affiliated Hospital Zhejiang University, Clinical Pharmacology Research Center, Hangzhou, China;* [3]*The First Affiliated Hospital Zhejiang University, Medical Oncology, Hangzhou, China;* [4]*Zhejiang Beta Pharma Inc., Research Center, Hangzhou, China*

**Background and Aim:** To assess the safety and tolerability of icotinib hydrochloride (BPI-2009H), a new selective epidermal growth factor receptor tyrosine kinase inhibitor (EGFR TKI), and to explore its pharmacokinetic (PK) and clinical activity in patients (pts) with advanced solid tumors, mainly with non-small cell lung cancer (NSCLC) after failure of prior platinum-based chemotherapy.
**Patients and Methods:** Oral icotinib (75, 100, 125, or 150 mg) was administered once 8 hours (Q8H) for 28-continuous day cycle until disease progression or undue toxicity. PK study were performed during cycle one (day 1 through 28). Enrollment required age $\geqslant$18 and $\leqslant$70 yrs, ECOG performance status 0−2 and adequate organ functions. Tumor response was assessed by RECIST. Plasma was sampled for PK analysis.
**Results:** 36 patients were enrolled. The common tumor types were NSCLC 33, breast cancer 2, and rectal cancer 1. 35 patients completed at least one cycle (28 days) treatment. Grade 3 dose-limiting toxicity (DLT) didn't occur even in 150 mg dose level and the maximum-tolerated dose (MTD) was not reached. Common grade 1−2 drug-related adverse events (AEs) were acne-like rash (42.3%), diarrhea (23.1%) and hematuria (7.7%), which were reversible on continuous treatment. No change in icotinib safety profile was observed with prolonged administration. Among the 33 pts with NSCLC, 32 pts were enrolled for clinical activity assess. At the 4$^{th}$ weeks, 13 pts had partial response (PR), 17 pts had stable disease (SD). At the 12$^{th}$ weeks, 12 pts had PR (1 pts lost), 13 pts had SD. At the 24$^{th}$ weeks, 7 pts had PR, 7 pts had SD, corresponding to a objective response rate of 21.9% (7/32) and disease control rate of 43.8% (14/32). From Dec 19 2007, we started the trial. The last patient finished recruitment on Jan 2nd 2009 and follow-up over 6 months. 6 pts remained on study now. PK analysis showed steady-state concentration exposured to icotinib 125 mg Q8H was obviously higher than it exposured to icotinib 100 mg Q8H. The $T_{1/2}$ was around 6 hours and Tmax was around 2 hours in all four different dose levels.
**Conclusion:** Oral icotinib was generally well tolerated, with manageable and reversible AEs, and showed positive clinical anti-tumor activities in patients with advanced NSCLC. The recommended dose for phase II/III study with icotinib is 125mg, Q8H.