because of toxicity or tumour progression, were randomized to receive daily oral doses of ZD6474 (300 mg) or gefitinib (250 mg) until disease progression or evidence of toxicity (part A). After a washout period of 4 weeks, patients were then eligible to switch to the alternative treatment, which continued until a withdrawal criterion was met (part B). The dual primary objective was evaluation of time to progression (TTP) and assessment of safety/tolerability.
Results: In part A, 168 patients from 35 centres were randomized to receive initial treatment with ZD6474 (n = 83) or gefitinib (n = 85). The results from the primary efficacy endpoint showed that the estimated median TTP was 11.9 weeks for ZD6474 and 8.1 weeks for gefitinib. The estimated hazard ratio of 0.632 corresponds to 58% prolongation of TTP for ZD6474 compared with gefitinib (95% CI, 11–125%; $P = 0.011$). The adverse event profile of ZD6474 was similar to that seen in previous trials, and included rash (grade 1/2, 25.3%; grade 3/4, 4.8%), diarrhoea (grade 1/2, 48.2%; grade 3/4, 7.2%) and asymptomatic QTc prolongation (all grade 1, 21.7%). There were no unexpected safety findings with gefitinib-treated patients. Results from secondary endpoints in part A, including response rate and survival, will be presented. Part B of the study is ongoing.
Conclusions: In this population of NSCLC patients, ZD6474, an inhibitor of VEGFR and EGFR tyrosine kinase activity, produced a statistically significant improvement in TTP when compared with the EGFR tyrosine kinase inhibitor gefitinib. These results support conducting further confirmatory trials.
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Poster presentations (Mon, 31 Oct)
Lung cancer

1125 POSTER

Improved disease-free durvival and dverall durvival by Navelbine (N) and Cisplatin (P) as adjuvant chemotherapy in completely resected (Stage I-III) Non Small Cell Lung Cancer (NSCLC): ANITA Trial. On behalf of Adjuvant Navelbine International Trial Association

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We are reporting the final results of a large randomized phase III trial (ANITA) demonstrating a survival benefit of vinorelbine-cisplatin as adjuvant chemotherapy for completely resected NSCLC pts. The ANITA study was designed to evaluate the impact on survival of adjuvant NP compared to observation in completely resected NSCLC pts.
Methods: completely resected pts were randomized to receive four cycles of adjuvant NP (N 30 mg/m^2/week for consecutive 16 weeks in combination with P 100 mg/m^2 on d1 every 4 weeks) or observation. Pts had to have histologically proven stage I (T2N0 only), II and IIIA NSCLC. Postoperative radiotherapy was predetermined by each center. ANITA was a multicenter, randomized (1:1) study, stratified by center, stage and histology. The main study end point was overall survival, assuming 5% alpha error and 90% power to achieve a 10% improvement on survival at 2 years, 400 pts had to be enrolled in each arm.
Results: Between 12/94 and 12/00, 840 pts (NP: 407, observation 433) were randomized from 101 centers in 14 countries. Median age 59 years (range 18–75), male 86%, WHO PS 0–1 95%, squamous cell carcinoma 59%, stage I, II, IIIA were 35%, 30% and 35% respectively. Lobectomy was performed in 58%, and pneumonectomy in 37%. Groups were well balanced with regards to age, gender, stage, histology and resection type. After a median follow-up >70 months, Overall and relapse-free survival were significantly different between arms; 65.8 and 36.3 months for NP versus 43.7 and 20.7months for observation (p value were 0.0131 and 0.002 respectively). Two, 5 and 7-year survivals were 68%, 51% and 45% in the NP arm versus 63%, 43% and 37% in the observation arm. The 5-year survival for stage I, II, IIIA were 62%, 52% and 42% in the NP arm versus 63%, 39% and 26% in the observation arm. The toxicity in the NP arm (WHO grade 3–4) was as expected and manageable; neutropenia 85%, febrile neutropenia 12.5%, nausea-vomiting 27%, constipation 5%, and peripheral neuropathy 3%. Seven pts (1.7%) died of drug-related toxicity. Cox Multivariate Analysis reported that Negative Nodal Status, Stage IB/II, Age <55yrs and chemotherapy were favorable prognostic factors for survival.
Conclusion: The ANITA results show that NP significantly improves relapse-free and long-term survival in completely resected NSCLC patients.

1126 POSTER

Symptom relief in patients with non-small cell lung cancer (NSCLC) after treatment with paclitaxel poliglumex (PPX, XYOTAX™): phase III trial results

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Background: Paclitaxel poliglumex (PPX; XYOTAX™) is a macromolecular drug conjugate linking paclitaxel to a biodegradable polymer, poly-L-glutamic acid. Because poly-L-glutamic acid links to the 2' hydroxyl of paclitaxel, a site crucial for tubulin binding, an inactive polymeric conjugate is formed. PPX is relatively stable in plasma; more than 97% of paclitaxel in circulation is present as the inactive conjugate thereby reducing systemic exposure to high concentrations of free paclitaxel. Consequently, PPX may have a more favorable toxicity profile than standard paclitaxel and improve symptom relief. Phase I/II studies indicate that PPX is active and generally well tolerated in high-risk patients (>70 years of age or poor performance status). Recently, enrollment has completed in 2 phase III trials examining single-agent PPX in patients with advanced NSCLC (STELLAR 2 and 4); the current analysis reports on patient benefit and symptom relief.
Materials and methods: STELLAR 2 included 849 patients and compared PPX to docetaxel in NSCLC patients with disease progression on or after a single platinum-containing regimen; STELLAR 4 included 477 poor performance status (PS2) patients and compared PPX to gemcitabine or vinorelbine. Patient reported symptoms were measured using FACT-LCS, a validated tool that consists of 7 questions that assess symptoms commonly reported by patients with lung cancer. FACT-LCS questions are rated on 5-point Likert-type scales ranging from 0 = "Not at All" to 4 = "Very Much." Patients completed the questionnaire within 3 days before each study treatment and 3 weeks after the last study dose. FACT-LCS response criteria were defined by exposure to drug and the change in FACT-LCS score from baseline over time: Worsened (2 or more point decline); Improved (2 or more point increase); Stable (1 point change or less).
Results: Fisher's exact test for equal proportion of patients achieving at least a 2-point increase in FACT-LCS score from baseline to week 3 will be performed. The Wilcoxon rank-sum test will be performed to assess change in FACT-LCS score from baseline over time. Summary statistics and 95% CI for the mean will be provided for each treatment arm at the scheduled visit week of the FACT-LCS questionnaire.

1127 POSTER

Phase II study of the EGFR tyrosine kinase inhibitor erlotinib in patients >70 years of age with previously untreated advanced non-small cell lung carcinoma

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Background: Chemotherapy for patients ⩾70 with advanced NSCLC is associated with survival benefits but with increased toxicity. Erlotinib has shown promising activity, and a tolerable side effect profile, in the treatment of patients who have failed prior chemotherapy. We have conducted a single center, phase II trial of erlotinib in patients ⩾70 years with previously untreated advanced NSCLC.
Methods: Patients who were chemotherapy-naïve, IIIB/IV, PS 0–2, were enrolled and treated with erlotinib, 150 mg p.o.q.d, until evidence of disease progression or toxicity. Median survival is the primary endpoint. Secondary endpoints include response rate, toxicity, quality of life (measured by LCSS), and gene sequencing for EGFR and K-ras mutations, and EGFR copy number (CN).
Results: From 3/03 to 2/05, 76 patients were treated; all were evaluable for survival and toxicity; 66 were evaluable for response. Demographics: M/F: 40/36; median age 75 (range 70–91); PS 0/1/2 13/55/8. Pathology: adenocarcinoma 51%; squamous 9%; adenocarcinoma with BAC features 8%; BAC 4%; other 28%. Smoking status: current/former/never: 4/64/8. Toxicity: Rash 75% (grade 1/2: 88%, grade 3:12%; grade 4: 0%); diarrhea 61% (grade 1/2: 98%; grade 3: 2%; grade 4: 0%). Other ⩾grade 3 toxicities: interstitial pneumonitis 3/76; anorexia 1/76; dehydration 2/76; hand–foot syndrome 2/76; elevations in PT/PTT 2/76; GI bleeding 2/76; hemoptysis