9010 ORAL

18F-FDG-PET 12 Weeks After Stereotactic Body Radiotherapy for Stage I Non-Small-Cell Lung Cancer Predicts Outcome

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Background: To investigate the prognostic value of post-treatment ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) 12 weeks after stereotactic body radiotherapy (SBRT) for stage I non-small-cell-lung cancer (NSCLC).
Materials and Methods: From November 2006 to February 2010, 132 medically inoperable patients with proven stage I NSCLC or FDG-PET-positive lung tumours were analyzed retrospectively. SBRT consisted of 60 Gy delivered at the 80% isodose, in 3−8 fractions. The maximum Standardized Uptake Value (SUV_{max}) of the treated lesion was assessed 12 weeks after SBRT using FDG-PET. Patients were subsequently followed at regular intervals using serial CT-scans. The association of post-SBRT SUV_{max} with local control (LC), mediastinal failure (MF), distant failure (DF), overall survival (OS), and disease specific survival (DSS) was examined.
Results: The median follow-up time was 17 months (range: 2−40 months). The post-SBRT median SUV_{max} was 3.0 (range: 0.55–14.50). The median lesion size was 25 mm (range: 9−70 mm). There were 6 local failures, 15 mediastinal failures, 15 distant failures, 13 disease-related deaths, and 16 intercurrent deaths (in total: 29 deaths). Using SUV_{max} 5.0 as a cut-off, the 2-year LC, MF and DF rates for the high and low SUV_{max} groups were 78.8% versus 97.1% ($P = 0.001$), 20.3% versus 13.0% ($P = 0.333$), and 28.8% versus 11.8% ($P = 0.078$), respectively. In the multivariate analysis, SUV_{max} >5.0 was a better predictor for LC than lesion size ($p = 0.025$). The 2-year OS and DSS rates for high and low SUV_{max} were 62.3% versus 80.7% ($P = 0.087$), and 73.6% versus 90.4% ($P = 0.037$) respectively.
Conclusion(s): Residual FDG uptake (SUV_{max} >5.0) predicts LC and DSS. A trend was found towards better OS for $SUV_{max} \leqslant 5.0$. A single FDG-PET scan at 12 weeks could be used to tailor further follow-up, according to the risk of failure.

9011 ORAL

Multicenter Analysis of High-resolution Computed Tomography and Fluorodeoxyglucose-positron Emission Tomography/Computed Tomography to Predict Malignant Grade of Clinical Stage IA Lung Adenocarcinoma

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Background: To understand malignant aggressiveness preoperatively is critical to choose suitable therapeutic strategies, such as sublobar resection, for patients with small lung cancers. The aim of this study was to examine the malignant biological behavior of clinical stage IA adenocarcinoma using HRCT, fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT), and a pathologic analysis in the setting of a multicenter study.
Methods: We performed HRCT and FDG-PET/CT on 502 patients with clinical T1N0M0 adenocarcinoma before they underwent curative surgery. We evaluated the relationships between clinicopathological characteristics and maximum standardized uptake values (maxSUV) on FDG-PET/CT, ground-glass opacity (GGO) ratio and tumour disappearance rate (TDR) on HRCT and component of bronchioloalveolar carcinoma (BAC) on surgical specimens, as well as between these and surgical outcomes. We used a phantom study to correct the serious limitation of any multi-institution study using PET/CT, namely a discrepancy in maxSUV values among institutions.
Results: Lymph node metastasis, lymphatic invasion, blood vessel invasion and pleural invasion was evident in 38 (8%), 76 (15%), 92 (18%) and 56 (11%) patients, respectively. Analyses of receiver operating characteristics curves identified an optimal cut-off value to predict pathologic high-grade malignancy (lymph node metastasis, lymphatic invasion, blood vessel invasion, or pleural invasion) of 2.5 for revised maxSUV, 20% for GGO ratio, 30% for TDR and 30% for BAC ratio. A significant difference in disease-free survival (DFS) was identified between patients whose adenocarcinoma had maxSUV $\leqslant$ 2.5 (n = 343; 3-year DFS rate, 96%) and >2.5 (n = 159, 3-year DFS rate, 77%; $p < 0.001$). Among patients with solid tumours showing GGO $\leqslant$50% and TDR $\leqslant$50% (n = 259), 19% (n = 27) and 15% (n = 22) of those with a maxSUV >2.5 (n = 143) had nodal metastasis and tumour recurrence, respectively, whereas those with tumours showing maxSUV $\leqslant$1.5 (n = 48) had neither nodal metastasis nor recurrence.
Conclusions: MaxSUV is a significant preoperative predictor for surgical outcomes. The findings of FDG-PET/CT in addition to HRCT are important to select therapeutic strategies for clinical stage IA adenocarcinoma of the lung.

Poster Discussion Presentations (Mon, 26 Sep, 11:00−12:00)

Lung Cancer

9012 POSTER DISCUSSION

A Phase Ib Study to Evaluate the PI3-Kinase Inhibitor GDC-0941 With Paclitaxel (P) and Carboplatin (C), With and Without Bevacizumab (BEV), in Patients With Advanced Non-small Cell Lung Cancer (NSCLC)

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Background: PI3K may be an important target in NSCLC as evidenced by genetic alterations in the pathway such as PIK3CA amplification and PTEN loss. The pathway has also been implicated as a mechanism for cell survival and resistance to chemotherapy. Preclinical NSCLC models show that concurrent dosing of GDC-0941 improved activity of taxanes, platins, and anti-VEGF therapy. This Phase 1b study aims to establish the safety and tolerability of GDC-0941 + C + P +/- BEV.
Methods: This 2-arm study is being conducted in 1L and 2L pts with advanced NSCLC. Arm A (GDC-0941+C+P) includes squamous (Sq) and non-squamous (NSq) pts who were ineligible for BEV. Arm B (G+C+P+BEV) includes NSq BEV-eligible pts. Pts received increasing doses of GDC-0941 (3 + 3 design) with P (200 mg/m^2) and C (AUC 6 mg/mL·min) (Arm A) and BEV (15 mg/kg, Arm B) every 3 weeks. In both arms, GDC-0941 was given PO qd on Days 1−14 of a 21-day cycle. While P+C were given for 4−6 cycles, GDC-0941 $\pm$ BEV were given until progression or toxicity. Study objectives were to evaluate safety and pharmacokinetics (PK), and to determine the maximum tolerated dose of GDC-0941 in both arms.
Results: As of 7 April 2011, 23 pts were enrolled into cohorts of 60, 100, 165, 250 and 330 mg GDC-0941 (Arm A) and cohorts of 100, 165, 250 and 330 mg GDC-0941 (Arm B). Treatment-related adverse events (TAEs) seen in $\geqslant$20% of pts (n = 20, safety cutoff 25 Feb 2011) were alopecia, asthenia, nausea, stomatitis, neutropenia, rash, decreased appetite (anorexia), leukopenia, peripheral neuropathy, paresthesia, epistaxis and arthralgia. All TAEs were Grade 1 (G1) and 2 except for neutropenia. G3 (15%) and 4 (10%) neutropenia AEs were not dose-limiting. GDC-0941 has shown dose-proportional exposures through 250 mg, similar to single-agent GDC-0941. PK characteristics of P and 6-OH-P were similar to historical profiles. Based on preclinical efficacy, an exposure consistent with a combination effect has been achieved at the 250 mg dose. A 330-mg dose cohort is currently under evaluation in Arms A and B with no DLTs thus far. Confirmed partial responses (PRs) were seen in 3 of 4 Sq pts, including 1 pt with a pathologic complete response (Arm A, 165 mg). Six of 9 (66%) NSq patients also had PRs (Arm B, 100–250 mg).
Conclusions: The combination of GDC-0941, P and C ($\pm$BEV) has been well tolerated at doses consistent with preclinical activity. Evaluation of 330 mg GDC-0941 + C + P$\pm$BEV is ongoing. Randomized studies are planned.

9013 POSTER DISCUSSION

Phase I Dose-escalation Study of AXL1717: a Novel Targeted Oral Insulin-like Growth Factor-1 Receptor (IGF-1R) Inhibitor and Its Implications for Patients With Non-small Cell Lung Carcinoma

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Background: The IGF-1R signaling pathway has been shown to be important for the growth and survival of many types of cancer cells. AXL1717 is a small molecule oral compound that has been optimized to