D7-03 Novel Therapeutics II, Thu, 12:30 - 14:15

A phase II study of erlotinib (E) and bevacizumab (B) in patients (pts) with previously untreated stage IIB/IV non-small-cell lung cancer (NSCLC)

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Background: In advanced NSCLC, E and B either as a single agent (E) or in combination with chemotherapy (B) have shown to improve survival. Combinations of targeted agents may prove to be effective and better tolerated than chemotherapy.

Methods: This is a multicenter 2-stage phase II study (Simon’s optimal design; p0=40%, p1=60%, α=0.05, β=0.20) with early stopping rule. The primary endpoint is non-progression (NPR) at 6 weeks. When 24/46 pts have NPR at 6 wks the treatment will be declared to have sufficient activity for further testing.

Results: Of 131 pts (PS 0-2) with advanced non-squamous NSCLC who had received no prior systemic anti-tumour therapy were treated with E (150mg/day) plus B (15mg/kg every 21 days) until disease progression or unacceptable toxicity. An imaging protocol including CT, DCE-MRI and FDG/H2O PET was performed at weeks -1,3 and 6.

Conclusions: E + B was well tolerated, with a low rate of grade 3/4 adverse events and no unexpected toxicities. The 75% progression rate justifies phase III testing in untreated advanced non-squamous NSCLC against platinum based chemotherapy. Updated data including correlation imaging studies will be presented.

D7-04 Novel therapeutics II, Thu, 12:30 - 14:15

Carbon ion radiotherapy for peripheral stage I non small-cell lung cancer

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Background: Some of the patients with stage I lung cancers can not be treated surgically because of low lung function and/or other reasons, development of non-surgical curative modalities are expected to decrease mortality from lung cancer. Carbon ion radiotherapy (CIRT) is a promising modality because of its excellent dose localization and high biological effects on a tumor. From 1994 to 1999, we conducted a phase I/II clinical trial for stage I non-small cell lung cancer (NSCLC) by using carbon ion beams alone. And demonstrated an optimal dose of 90GyE in 18 fractions over 6 weeks and 72GyE in 9 fractions over 3 weeks, achieving more than 95% local control with minimum pulmonary damage. In the present study, we conducted a phase II clinical trial for stage NSCLC to determine the local control and the survival rates.

Methods: One hundred twenty-nine patients with 131 primary lesions were treated from 1999 to 2003 in National Institute of Radiological Sciences, Research Center Hospital for Charged Particle Therapy, Japan. The patients consisted of 37 females and 92 males, with a mean age of the patients 74.5 years. The T1 and T2 numbers were 72 and 59, respectively, and the average tumor size in diameter was 31.5 mm. By histology, the tumors broke down into 85 adenocarcinomas, 43 squamous cell carcinomas, two large cell carcinomas and one adenosquamous cell carcinoma. A primary tumor was treated with carbon beam alone using the fixed total dose of 72GyE in 9 fractions over 3 weeks, or 52.8GyE for stage IA, 60GyE for stage IB over one week. Most of targets were irradiated from obliquely from four directions. A respiratory-gated irradiation system was used for irradiation in each case. Local control and survival were determined by using the Kaplan-Meier method and the data were statistically processed by using the log-rank test (the significance level was 0.05).

Results: The cumulative local control rate for all lesions was 94.7% at 58 months after CIRT. There was no statistical difference in the local control rate between T1 and T2 (p=0.061), and between the histologies (squamous cell carcinoma vs. non-squamous cell carcinoma) (p=0.077). Overall 5-year survival rates after CIRT were 68.7% in stage IA (n=69), 46.4% in stage IB (n=56). No toxic reactions were observed in the skin and no adverse effects worse than grade III were detected.

Conclusions: Carbon ion beam radiotherapy, a new therapy modality with superior benefits in terms of QOL and ADL, has been proven to be a valid alternative to surgery for stage I NSCLC and to offer particular benefits especially for the poor surgical candidates.