9121 POSTER

A Multi-center, Open, Randomized, Phase II Study to Investigate the Sequential Administration of Docetaxel and Intermittent Erlotinib Versus Erlotinib as a Second-line Therapy for Advanced Non-small Cell Lung Cancer (NSCLC)

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Background: Patients (p) with advanced NSCLC have few treatment options after progressing to 1st-line platinum doublet chemotherapy (PDC). Several preclinical and phase I studies have suggested that sequential administration of erlotinib (E) and docetaxel could avoid possible negative interactions and optimize the benefit obtained against NSCLC.
This randomized phase II was designed to address the clinical benefit obtained with the use of sequential administration of docetaxel and intermittent E.
Methods: 70 p with advanced NSCLC progressing to previous PDC for advanced disease were randomized (1:1): Group A (n = 34): Docetaxel 75 mg/m^2 day 1 and intermittent E (day 2−16), up to 4 cycles, followed by E in monotherapy; Group B (n = 36): E in monotherapy.
Treatment was administered until unacceptable toxicity or disease progression. Primary endpoint: rate of p free of progression at 6 months; secondary endpoints: progression-free survival (PFS), overall survival (OS), disease control rate (DCR) and safety.
The study has completed enrolment. Data from 32 p included are shown: 15 in Group A/17 in Group B.
Results: Baseline characteristics: non-adenocarcinoma (71%), current/former smokers (93.7%), male (90.6%) and stage IV (83.9%). 6 months PFS: 14.3% in the sequential arm. PFS: 2.3 months (m) in Group A (95% CI 1.9−3.1) and 3.1 m in Group B (95% CI 2.0−4.5). Median OS: 4.9 m (95% CI 2.7 − -) in group A, slightly different than in Group B (6.0 m; 95% CI 2.5−6.0). DCR: 25% in the experimental group (95% CI 0.5–49.5) whereas in the D one was 50% (95% CI 23.8–76.2). Adverse events (AEs), including skin rash and diarrhea, were all generally tolerable. Although the incidence of treatment-related AEs was higher in Group A than in B, AEs leading to dose reduction were more common in the E arm (11.8% vs. 6.7%).
Conclusions: Although this preliminary analysis shows no impact in the PFS and OS of this sequential treatment, data from 6 months PFS of the sequential arm may suggest a potential benefit of the combination. Final data of the primary endpoint from the whole population will be presented during the meeting.

9122 POSTER

Efficacy of Gefitinib in Patients With Epidermal Growth Factor Receptor Mutation Positive Advanced Non-Small-Cell Lung Cancer − a Metaanalysis of Randomized Controlled Trials

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Background: Lung cancer is the leading cause of malignancy-related death worldwide. Having a role in cellular proliferation, inhibition of apoptosis, metastasis and chemoresistance, overexpression of epidermal growth factor receptor (EGFR) tyrosine kinase (TK) is evident in most patients with non-small-cell lung cancer (NSCLC) that accounts for 80% of all lung cancers and associated with a dismal prognosis. Therefore, the present metaanalysis was performed to review the recent advances with the selective oral EGFR TK inhibitor gefitinib in NSCLC.
Material and Methods: We searched MEDLINE and ClinicalTrials.gov using the keyword “Gefitinib”. Of more than 1000 published reports retrieved, older studies and studies with diverse methodology were excluded while the primary reports of interest were the RCTs published since 2005 after which gefitinib use was intensified. Hence, three recent studies concerning the effect of gefitinib on NSCLC were identified to be relevant for the meta-analysis based on their similarity in terms of study design (Table 1). For the effect estimates, hazard ratio (HR) was used with the 95% confidence intervals (CIs).
Results: The HR (95% CI) of the meta-analysis of **0.410 (0.341; 0.492)** demonstrated that in patients who were positive for EFGR mutation, PFS was significantly longer among those who received Gefitinib than among those who received platin derivative/taxane combination. In other words, a 2.44 times longer PFS time was obtained with gefitinib in these patients.
Conclusions: The HR obtained with this metaanalysis more strongly supports the efficacy of gefitinib, and stresses on the importance of EGFR mutation test and gefitinib use in routine practice of NSCLC.

Table 1. Summary of gefitinib efficacy data in patients with EGFR mutation positive advanced NSCLC obtained in randomized clinical trials included in this metaanalysis

	Patient selection	Comparator and sample size	Primary end point	Response rate	HR (95% CI)
Mok, 2009 [1]	Asian	132 Gefitinib versus 129 carboplatin−paclitaxel	PFS	71.2 vs 74.3, p < 0.001	0.48 (0.36; 0.64)
Maemondo, 2010 [2]	<75 of age	114 Gefitinib versus 114 carboplatin−paclitaxel	PFS	73.7 vs 30.7, p < 0.001	0.30 (0.22; 0.41)
Mitsudomi, 2010 [3]	Asian	86 gefitinib versus 86 cisplatin−docetaxel	PFS	62.1 vs 32.2, p < 0.001	0.49 (0.34; 0.71)

PFS: Progression free survival

References

[1] Mok TS, et al. N Engl J Med 2009;361:947−57.
[2] Maemondo M, et al. N Engl J Med 2010;362:2380−8.
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9123 POSTER

Final Results of a Phase II Study of Gefitinib as First-line Treatment in Elderly Epidermal Growth Factor Receptor-mutated Patients With Advanced Non-small Cell Lung Cancer − Gefitinib for Elderly Patients With Lung Adenocarcinoma

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Background: Many studies have proven the efficacy of gefitinib in non-elderly patients. However, Data on the feasibility of gefitinib therapy in elderly patients (75 years or older) with non-small-cell lung cancer is limited. This phase II study aimed to investigate the efficacy and usefulness of gefitinib therapy as a first-line treatment for elderly patients with advanced lung adenocarcinoma with epidermal growth factor receptor (*EGFR*) mutations.
Methods: Chemotherapy-naïve advanced Japanese lung adenocarcinoma patients aged 75 years or older with a stage IIIB/IV (ECOG of 0−2) and activating *EGFR* mutation were enrolled. Patients were administered gefitinib (250 mg) once daily until progression or unacceptable toxicity. Responses were determined using RECIST with radiographic evaluations. The primary endpoint was response rate (RR), and secondary endpoints were disease control rate (DCR; defined as complete response [CR] plus partial response [PR] plus stable disease [SD]), progression-free survival (PFS), overall survival (OS), and toxicity profile. Response rate was set at 75% in enrolled patients and a rate of 30% as the lower limit of interest, with α = 0.05 and β = 0.1. The estimated accrual number was at least 12 cases or more. This trial is not sponsored by the pharmaceutical industry, government or any other source that would cover the cost of the treatment.
Results: Between April 2008 and November 2009, seventeen lung adenocarcinoma patients were enrolled. Overall RR was 59% (95% confidence interval [CI]: 33% to 81%), with 2 patients achieving CR and 8 PR. Stable disease was noted in 5 patients, and DCR was 88% (95% CI: 62% to 98%). The median follow-up time was 18.6 months (range: 0.5 to 30.6 months). Median PFS was 14.2 months (95% CI: 2.2 to 23.6 months), and median OS had not yet been reached. The median duration of response was 10.7 months (range: 2.8 to 26.4 months). Major grade 3 toxicities were skin rash (12%) and increased levels of aspartate aminotransferase or alanine aminotransferase (18%).
Conclusion: In elderly patients harboring activated EGFR mutation, gefitinib is well tolerated and shows a promising activity.
This study is registered with UMIN-CTR
[identification number UMIN000002783].

9124 POSTER

Nimotuzumab in Combination With Chemotherapy in the Patients With Advanced Non-small Cell Lung Cancer

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Background: Nimotuzumab, a humanized anti-EGFR monoclonal antibody, has demonstrated well tolerate anti-cancer efficacy. Therefore, we