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.
[3] Mitsudomi T, et al. Lancet Oncol 2010;11:121−8.

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

designed the study for evaluate the role of Nimotuzumab in combination with chemotherapy in the patients with advanced non-small cell lung cancer (NSCLC).
Material and Methods: A retrospective review of the clinical data of Cancer Hospital, Tianjin Medical University identified 37 NSCLC patients who received Nimotuzumab in combination with chemotherapy from January 2009 to October 2010. Of 37 patients, 12 patients were in stage IIIB, 25 patients in stage IV; 24 patients received platinum-based chemotherapy in combination with Nimotuzumab, 13 patients received nonplatinum-based chemotherapy in combination with Nimotuzumab; 10 patients administered Nimotuzumab plus chemotherapy as first-line regimen, 23 patients as second-line regimen, 4 patients as third-line regimen.
Results: Of the 37 advanced NSCLC patients who received Nimotuzumab in combination with chemotherapy, the total number of chemotherapy were 137 cycles (mean 3.7 cycles); complete remission (CR) in one patient, partial remission (PR) in 9 patients, stable disease (SD) in 16 patients, progressive disease (PD) in 11 patients. The response rate (RR) was 27%, clinical benefit rate (CBR) was 70.3%. The main side effects were bone marrow depression and gastrointestinal reactions. Acneiform rash of grade I was found in one patient.
Conclusions: The regimen of Nimotuzumab in combination with chemotherapy could improve response rate and was well tolerated in the patients with advanced non-small cell lung cancer.

9125 POSTER

Role of Chemotherapy in ECOG Performance Status 3 Small Cell Lung Cancer − a Single Centre Study

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Background: The purpose of this study is to evaluate the treatment and its impact on survival of small cell lung cancer (SCLC) patients (pts) with ECOG Performance status (PS) 3 presenting to a single UK Cancer Network. There is no standard treatment policy for the pts with SCLC presenting with ECOG PS 3. These pts may experience symptomatic and survival benefits with chemotherapy (CT) but are at a greater risk of early treatment related death. Management of these patients vary from best supportive care to single agent or combination CT.
Methods: Retrospective analysis of all PS3 pts diagnosed with SCLC presenting from Jan 2005 to Dec 2009 at Merseyside & Cheshire Cancer Network. Data were prospectively recorded using an electronic minimum data set.
Results: A total of 978 pts were diagnosed with SCLC. Out of those 219(22%) pts presented with PS 3. Median age was 71 yrs (38−91 yrs). There were 117(53%) female and 102(47%) male pts. 182(83%) had extensive stage disease and 34(16%) had limited stage disease. Majority of pts (N = 182, 65%) did not receive any CT.
Median overall survival was 3 months (mo). Median survival for those who had CT was 6 mo (95% CI 3.70–8.29) compared to 2 mo (95% CI 1.71–2.28) for those who were not treated (p-value <0.01). 21(27%) pts died within 30 days of receiving chemotherapy. Median survival for pts receiving platinum based combination CT (carboplatin and etoposide, N = 40) was 7 mo (95% C.I 2.6–11.4), for single agent carboplatin (N = 31) was 5 mo (95% C.I 2.7–7.37) and for oral Etoposide (N = 6) was 2 mo (95% C.I 1.4−2.6).
Clinical factors favouring longer survival were female gender, limited stage disease, absent or single site visceral metastases, weight loss of less than 5% of total body weight and minimal co-morbidities.
Conclusion: Overall survival is poor and treatment related early deaths are not uncommon in PS 3 SCLC patients but better selection of patients for CT can improve this. Pts benefited the most were female gender, with limited stage disease and those treated with combination chemotherapy. The optimum CT regimen remains to be defined.

9126 POSTER

Anaemia Risk With Anti-EGFR Agents in Advanced Non Small Cell Lung Cancer − a Meta-analysis of 10 Trials

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Background: Anaemia is a prevalent event in advanced non small cell lung cancer (NSCLC) patients related to the disease and to the myelosuppressive effect of chemotherapy. Are the widely used anti-epidermal growth factor receptor (EGFR) agents, additional potential causes of treatment-related anaemia?
Patients and Methods: Databases from PUBMED until December, 2010 were searched. Eligible studies included prospective randomized controlled trials in which standard anti-neoplastic therapy (or best supportive care) was administered with and without the use of erlotinib, gefitinib or cetuximab, with available data of anemia. Summary incidence rate, relative risk (RR), and 95% confidence interval (CI) were calculated employing fixed- or random-effect models based upon the heterogeneity of the included studies. RevMan v. 5.1 (Cochrane IMS) has been used for statistical analysis.
Results: A total of 5700 patients from 10 studies in advanced NSCLC were included for analysis. Among all patients the incidence of anemia was 18% (95% CI: 16.55–19.6%). In comparison with standard therapy, anti-EGFR agents significantly increased the risk of anemia with an RR of 1.49 (95% CI 1.03–2.16, p = 0.03 according to random effect model). Considering all studies with erlotinib and gefitinib, the risk of anaemia is even higher (RR 2.05; 95% CI 1.24–3.39, p = 0.005 according to random effect model). In trials comparing only erlotinib or gefitinib plus chemotherapy with chemotherapy alone the RR of anaemia was 1.92 (95% CI: 1.16−3.2; p = 0.01 according to random effect model).
Conclusions: Anaemia is a frequent event with anti-EGFR agents in particular with oral agents as gefitinib and erlotinib. This metanalysis shows that they exert an additive effect in NSCLC patients because they almost doubled the risk of development of anaemia compared to chemotherapy alone. Prevention and early treatment, in a setting where anaemia is already a common event, is crucial.

9127 POSTER

Phase II Study of Erlotinib Plus Gemcitabine in First Line Treatment of Poor Prognosis (ECOG PS 2) Advanced Non-small Cell Lung Cancer Patients

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Background: The combination of Erlotinib with chemotherapy has been a touchstone in advanced (IIIB and IV stages) NSCLC patients'treatment. The majority of clinical studies exclude patients with poor prognostic status (ECOG 2) and in this situation there are no clinical evidence for treatment of this patients.
Patients and method: Between August 2008 and April 2010, 20 patients with NSCLC stage IIIB (7pts) and stage IV (12 pts) with ECOG PS 2 have been randomized in the study; one patients wasn't included in final analysis; patients'characteristics were: male(16pts), female (3pts), median age 64 (range 47−75), smoking status: 3 non-smokers, 13 smokers, 3 non-declared, histological type: squamos cell carcinoma (7 pts), adenocarcinoma (9 pts), BAL (1pt), large cell carcinoma (2pts).
Study treatment: Gemcitabine1000 mg/m^2 days 1−8-15 plus Erlotinib 150 mg/day in first line treatment of NSCLC. The treatment was administreated for 6 cycles or until disease progression or unacceptable toxicity. Study objectives: primary objectives − response rate, TTP; secondary objectives − OS, safety and tolerability.
Results: The overall response rate was 15.8%, CBR was 36.84%, median TTP − 15 weeks (95% CI: 7−36), median OS − 39 weeks (95% CI: 27- 51). The grade IV CTC toxicity was represented by diarrhea (1pt), respiratory infection (1pt), thrombocytopenia (1pt) and anaemia (1pt).
The concomitant diseases were recorded in every patient: COPD (3pts), arterial hypertension (9 pts), cardiac ischaemic disease (4 pts), congestive heart failure (3 pts), type II diabetes mellitus (2 pts), cirrhosis (2 pts), chronic renal failure (1pts), artheriopathy (3 pts), asthma (1 pts), prostate cancer (1pts), sarcoidosis (1pt), hyperthiroidy(1pt), dislipidemia (3pts).
Conclusions: Taking into account the publised clinical studies regarding chemotherapy treatment of the same patients population (V. Gebbia et al. 2005) we observed that gemcitabine plus Erlotinib have superior response rate and superior overall survival with acceptable tolerability. This treatment combination represent a treatment option for patients with advanced NSCLC with ECOG PS 2, regardless by the pathological type, gender or smoking status. Maybe a phase III clinical study could bring more clinical evidence.

9128 POSTER

Prospective Multicenter Study of Pemetrexed and Carboplatin Combination Followed by Maintenance Pemetrexed in Chemo-naïve Patients With Non-squamous Non-small Cell Lung Cancer

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Background: Platinum-based chemotherapy is the standard first-line treatment for advanced non-small cell lung cancer (NSCLC); furthermore,