Phase II trial of pemetrexed and gemcitabine as first-line chemotherapy for elderly and/or poor performance status patients with stage IIIb/IV non-small cell lung cancer (NSCLC)


Background: The combination of Pemetrexed (PEM) and Gemcitabine (GEM) in the treatment of locally advanced or metastatic NSCLC has shown synergy in both preclinical and clinical studies with a favorable toxicity profile compared to other doublets. Late-stage and symptomatic diagnosis in elderly patients remains an increasingly common problem. This study was designed to evaluate the efficacy of this doublet as first-line therapy for advanced NSCLC in the most difficult to treat patients, i.e. older patients and those with poor performance status. The goal of this novel doublet regimen is to preserve the activity of two-drug combinations while minimizing toxicity in an ‘at-risk’ population.

Methods: Patients with age > 65 and ECOG 0-2 or age < 65 and ECOG of 2, with locally advanced or metastatic (measurable stage IIIb/IV) NSCLC by RECIST criteria were treated with biweekly cycles of PEM 500mg/m² IV over 10 minutes, followed by GEM 1500 mg/m² IV over 30 minutes on Day 1. Cycles were repeated every 2 weeks with a maximum of 12 cycles for stable or responding patients. All patients received vitamin B12 1000 µg and folic acid 1000 mg 7 days prior to initiation of treatment and continued through treatment.

Results: 45 patients were enrolled to this study. The median age is 72 (range 46-88). Five patients had stage IIIB and 40 stage IV, median number of sites of disease is 2. 62% are male. Patient performance status was as follows: ECOG 0=5, ECOG 1=27, ECOG 2=13 patients. Overall, 22 pts experienced a Grade 3 or 4 AE. Seven patients had grade 3 or 4 neutropenia with 2 patients having febrile neutropenia. There were 2 patients with grade 3 or 4 anemia, and one with thrombocytopenia. 30 patients were evaluable for best overall response, with 1 achieving CR (3%), 6 with PR (20%), 16 with SD (53%) and 7 with PD (23%). Overall, clinical benefit (CR+PR+SD) was seen in 76% of patients.

Conclusion: Pemetrexed and Gemcitabine in combination on a biweekly schedule has substantial activity with a favorable toxicity profile for elderly patients with advanced NSCLC. Overall response rates and clinical benefits are comparable to contemporary platinum containing doublet regimens.

Activity of intravenous Topotecan in patients with advanced non-small cell lung cancer pre-treated with platinum and taxanes: Results of the first analysis

Villanueva, Noemí; Esteban, Emilio; Llorente, Beatriz; Fernández, Yolanda; Jimenez, Paula; Capelan, Marta; Fra, Joaquín; Vieitez, Jose María; Muñiz, Isabel; Lacave, Angel J. Hospital Universitario Central de Asturias, Oviedo, Spain

Background: Topotecan, a semi-synthetic camptothecin analogue with topoisomerase I interaction has shown to be an active agent in the treatment of advanced refractory lung cancer and ovarian cancer. In this report, experience with this drug is described when used as a single agent in patients with advanced NSCLC refractory to chemotherapy regimens containing at least platinum and taxanes.

Material and Methods: Twenty-four patients (pts) with NSCLC refractory to previous chemotherapy and KI ≥60% were included in the study showing the following features: median age of 52 years (range 43-69) and Karnofsky PS of 70 (50-80), 21 were male and 3 female. Fifteen (62%) pts had adenocarcinoma, six (25%) squamous cell and three (13%) undifferentiated carcinoma. The median number of disease sites and prior regimens received were two in both cases. Topotecan was given at a dose of 1.25 mg/m² IV. daily for five days, repeated every 21 days until progression disease, maximal response or intolerable toxicity occurred.
Results: After 52 cycles administered, pts received a median of 2 cycles of treatment (1-6). All patients except one were considered evaluable for toxicity, with the recording of five episodes of (22%) nausea/vomiting grade 1-2 and one (4%) of asthenia grade 1. Four (17%) patients developed anemia grade 2-3 and neutropenia grade 1. Two additional patients (9%) had neutropenia grade 2 and one (4%) grade V. Among twenty evaluable pts for activity, one (4%) showed partial response, seven (29%) stable disease and twelve (50%) progression disease. Median time to progression and overall survival are 54 (12-210) and 60 (12-485) days respectively.

Conclusion: At this time of evaluation, intravenous Topotecan with this schedule and dose shows promising activity. The accrual still continues until the planned sample size following the Simon Two-stage design.

P2-319 NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4
Taxotere as salvage chemotherapy in Chinese patients with advanced NSCLC who have failed or relapsed after the gefitinib target treatment
Wu, Yi-Long; Yang, Jin-Ji; Huang, Yu-Juang; Liao, Rl-Qiang; Zhou, Qin; Huang, Yi-Sheng; Xu, Chong-Rui

1 Lung Cancer Research Institute, Guangdong Provincial People's Hospital, Guangzhou, China
2 Guangdong Provincial People's Hospital, Guangzhou, China

Background: This Phase II study was conducted to evaluate the efficacy and toxicity of docetaxel single agent in salvage therapy for patients with advanced non-small cell lung cancer (NSCLC) who failed to respond or relapsed after the gefitinib.

Methods: Patients with histologically confirmed and progressive NSCLC after gefitinib were eligible for this study. Performance status of 0-1 and adequate organ function were required. Patients were treated with docetaxel 75 mg/m² intravenously for 30 min repeated every 3 weeks until disease progression or intolerant toxicity.

Results: Twenty patients were eligible for this study. The TTP for iesraa was 12 months. Average 2.9 cycles taxotere were given. Hematologic toxicity was mild and with the major toxicity of anemia and peripheral neuropathy. The overall response rate (ORR) was 15% and disease control rate was 40%. The median survival time (MST) for all patients was 542 days (95% CI, 238.2-845.7), TTP was 3.5 months and the 1 year survival was 50.2%.

Conclusions: Docetaxel appeared to be well tolerated as salvage therapy for patients with NSCLC who failed to gefitinib.

P2-320 NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4
Marked response to a cisplatin/docetaxel/temozolomide combination in a heavily pre-treated lung cancer patient with a metastatic large cell neuroendocrine tumour.
Gounaris, Ioannis; Rahamim, Joe; Shivasanak, Siva; Earl, Sarah; Lyons, Bruce; Yianmakis, Dennis

Plymouth Hospitals NHS Trust, Plymouth, UK

Introduction: Large cell neuroendocrine carcinoma (LCNEC) is rare and differs from other non-small cell lung carcinomas (NSCLC) in that it has a particularly aggressive clinical behaviour with poor prognosis. We report a dramatic response in body and brain metastases in a heavily pre-treated LCNEC patient receiving a fourth-line combination of cisplatin / docetaxel / temozolomide.

Case Report: A 52-year-old female initially presented with increasing breathlessness and superior vena cava obstruction. Histology showed LCNEC. Computed tomography showed bulky mediastinal disease. Over the next 6 months she received two lines of chemotherapy [cisplatin / etoposide (stable disease), followed by carboplatin / paclitaxel / radiotherapy (good partial response)]. She progressed 8 months from diagnosis with brain metastases (one 5cm diameter). She had a partial response to whole brain radiotherapy, but soon after completion she was commenced on gefitinib for progressive intraabdominal disease. She progressed on gefitinib with marked clinical deterioration and massive radiological progression in mediastium, liver, adrenal and brain (12 months from presentation). After a request for more treatment a cisplatin, docetaxel and temozolomide triplet combination was administered [cisplatin 40mg/m² iv day 1; docetaxel 25 mg/m² iv days 1, 8, 15; temozolomide 150mg/m² orally days 1-5, every 4 weeks]. The regimen was based on a single previous case report in metastatic NSCLC and the patient received four cycles of treatment. An excellent symptomatic and radiological response (including the brain metastases) was seen, with a marked improvement in her quality of life that enabled her to return to full activity. Unfortunately the disease started to progress again four months later and the patient died 20 months from presentation.

Discussion: LCNEC is a rare tumour. The tumour is traditionally considered to fall within the category of poorly differentiated NSCLC. However, outcomes are similar to SCLC, including a propensity for early brain metastases. This is the second report in the literature on the use of this specific chemotherapy combination in NSCLC and the first report of this cisplatin / docetaxel / temozolomide regimen in LCNEC. This triplet is a well-tolerated novel outpatient combination chemotherapy regimen that treats both systemic and intracranial disease. The growing evidence form case series and phase II trials on the use of temozolomide containing regimens in patients with recurrent or progressive brain metastases from solid tumours will be reviewed. In patients who have failed WBRT palliative care was usually the only available management option. For fit patients temozolomide singly or preferably in combination may offer a real alternative.

P2-321 NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4
Efficacy of cisplatin and vinorelbine in patients with metastatic NSCLC
Yilmaz, Ufuk; Halilcolar, Huseyin; Yildirim, Yasemin; Yapicioglu, Sena; Unsal, Ipak; Mahlec, Ceyda

Suat Sener Chest Disease and Surgery Training and Research Hospital, Izmir, Turkey

Background: Chemotherapy for advanced NSCLC has gained widespread acceptance since it was demonstrated that cisplatin-based chemotherapy improved survival and quality of life. The aim of this study is to evaluate the feasibility in terms of overall survival, response rate and toxicity of the cisplatin-vinorelbine in Turkish patients with metastatic NSCLC.

Methods: In this prospective study, ECOG performance 0-1, chemotherapy-naive stage IV NSCLC patients (pts) were treated with cisplatin (75 mg/m², d1, IV) and vinorelbine (30 mg/m², d1 and d8, IV) every 21 days until progression or unacceptable toxicity for a maximum of 6 cycles in single center. Tumor responses were evaluated by WHO criteria. Survival was calculated with the Kaplan-Meier method. Eight