Title	The combined use of gemcitabine and ifosfamide in patients with Stage III or IV non-small cell lung cancer (NSCLC)
Author(s)	Lam, CL; Lam, WK; Ip, MSM; Tsang, KWT; Lam, B; Yan, CPK; Ho, JCM; Ip, S; Wong, MKY
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C-RC-2

Establishment of HKU Lung Cancer Cell Lines in Hong Kong - An Ongoing Conjoint Effort and Progress Report

CL Lam, WK Lam, MP Wong,* LP Chung,* SW Chiu,# WS Chau#
*Univeristy Department of Medicine and Department of Pathology, The University of Hong Kong; #The Cardiothoracic Surgical Unit, The Grantham Hospital

Introduction: Lung cancer accounts for the majority of cancer deaths in Hong Kong. There is an unusually high incidence of lung cancer in non-smoking women in Hong Kong but the pathobiology of these cancers are not fully understood. Commercially available sources of lung cancer cell lines seldom provide details such as the smoking history of the patient. The establishment of lung cancer cell lines, particularly from non-smokers, would provide a handle for the study of the genetics, biology and potentials for therapeutic manipulation in these cancers.

Methods: Surgically resected primary lung cancer specimens, as well as pleural and pericardial fluid samples from patients with lung cancer at both the Queen Mary Hospital and the Grantham Hospital are collected. ACL4 and RPMI with variable concentrations of fetal calf serum are used as medium. Tumour specimens are also transplanted into nude mice. Tumour cells obtained will be continuously passaged in the respective culture medium or as tumour xenograft in nude mice. Characterization of cultured cells or xenograft are performed with immunohistochemical staining, electron microscopy and comparative genomic hybridization (CGH).

Results: Two new cell lines (HKULC1 and HKULC2) (from smokers/non-smokers) from pleuropericardial fluid specimens had been established with constant growth kinetics. Immunohistochemical staining showed immuno-positivity for CK7 and CEA, while staining for CK20, TTF-1, calretinin, ER and PR were negative. Further characterization with electron microscopy and CGH is in progress. Two samples from resected primary tumours have been maintained by passaging in nude mice and further characterization would be performed.

Conclusion: There is a higher success rate of establishment of lung cancer cell lines from tumour metastasis in pleural or pericardial fluid than from primary resected lung cancers. Further collection and establishment of lung cancer cell lines will provide substrate to support other molecular and therapeutic studies in lung cancer in Hong Kong Chinese.

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C-RC-3

The Combined Use of Gemcitabine and Ifosfamide in Patients with Stage III or IV Non-Small Cell Lung Cancer (NSCLC)

CL Lam, WK Lam, MSM Ip, KWT Tsang, B Lam, C Yan, JCM Ho, S Ip, MKY Wong
University Department of Medicine, Queen Mary Hospital

Introduction: Gemcitabine acts as a nucleoside analogue and has been found in phase I clinical trial to have a response rate of up to 33% when used as monotherapy for NSCLC. Traditional cisplatin-based chemotherapy is often complicated with severe myelotoxicity. In this study, we hypothesize that this new therapeutic combination of Gemcitabine and Ifosfamide in patients with NSCLC may give rise to a relatively less myelotoxic chemotherapy regime with a satisfactory response rate.

Methods: Patients with unresectable stage III or IV NSCLC who have not received previous chemotherapy were recruited with informed consent. A combination of Gemcitabine ($1g/m^2$, day 1 and 8) and Ifosfamide ($3g/m^2$, day 1) was administered in 4 weekly cycles. Recruited patients were assessed at the end of each cycle, with respect to the Karnovsky performance score, blood parameters and chest X-ray, before proceeding to the next cycle. Patients with satisfactory response or static disease will have a maximum of six cycles if tolerated. Any clinical or imaging evidence of disease progression on chemotherapy will lead to termination from study.

Results: There were 21 patients (M:F=11:10, mean age 54.27 ± 9.41, stage IIIA/IIIB/IV=1/10/10) who had completed at least 2 cycles with evaluable response, with 3/21 (14.3%) showed partial response, 8/21 (38%) showed static disease and 10/21 (47.6%) showed progressive disease requiring termination from study. Five patients (23.8%) needed dose reduction or omission for WHO Grade I–III neutropenia and all of them recovered spontaneously without developing severe life-threatening sepsis. One patient (4.8%) had mild cystitis symptoms requiring cycle delay for the sixth cycle. Other patients managed to complete each cycle on time targeted dose administration.

Conclusion: The combined use of Gemcitabine and Ifosfamide in chemo-naïve advanced NSCLC patients did not give rise to better response rate as previously reported as monotherapy, although the regime seems to be well tolerated without life-threatening complication in this study.