



# Practical Management of Non-Small Cell Lung Cancer

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Hong Kong saw just over 4,000 new cases of lung cancer in 2004. It is the first-ranking incident cancer in men and number 3 in women. However it tops the cancer mortality chart, responsible for over 3,500 deaths in the same year. Most, around 90%, are non-small cell lung cancers (NSCLC). Most male lung cancer patients are smokers while most female are non-smokers. The aetiology of non-smoking female having lung cancer is still a hot topic of epidemiological studies.

## Diagnosis and Staging

Lung cancers tend to present in an advanced stage. Most adenocarcinomas are situated in the periphery of the lung. Thus they seldom produce classical textbook symptoms like cough, shortness of breath, haemoptysis, which are more 'central' or 'proximal' airway symptoms. Nowadays non-small cell carcinomas tend to present with constitutional symptoms like weight loss, anorexia and sometimes with advanced disease like pleural effusion and distant metastasis. These non-specific symptoms may evade early detection by clinicians.

Bronchoscopy becomes less and less useful for obtaining pathological diagnosis, since the tumours are in the peripheral airways. More and more transcutaneous biopsies under CT scan guidance are performed. In some instances mediastinoscopy is used to biopsy enlarged mediastinal nodes. Supraclavicular adenopathy, if present, are also convenient sites to obtain cytological (fine needle aspiration) or histological (core biopsy) diagnosis. Sputum cytology, or in the case of presence of pleural effusion, pleural cytology are also sources for pathological diagnosis.

The most important point for staging is to determine the mode of treatment. Stage I is primary lung cancer without metastasis. Stage II permits hilar adenopathy only. Stage III denotes presence of pleural effusion or mediastinal adenopathy. Stage IV means presence of distant metastasis, including intra-pulmonary metastasis.

The most favourable situation would be stage I or II lung cancer which would be treatable by surgery. These are few and far between. Most are incidental findings on radiological imaging for other purposes. Screening for lung cancer, using high resolution computerised tomography, remains a controversial issue, with the effect on mortality remaining to be proven. The 'who, when, with what, how often...' are still undetermined.

The practical way to stage lung cancer is determined by

the starting point at diagnosis. If distant metastasis is obvious there is no point to use highly sophisticated staging modalities. If one may be dealing with early, operable lung cancer, then thorough evaluation is necessary. Useful methods include high resolution CT thorax, PET-CT scan and mediastinoscopy. The common theme is to determine whether metastatic mediastinal nodes are present.

## Treatment for Stage I and II NSCLC

Given stage I and II non-small cell lung cancer patients, the next determinant would be whether surgical treatment is appropriate. Important factors include age, performance status and co-morbidities. Adequate lung function is an obvious pre-requisite. Pneumonectomy, lobectomy with mediastinal lymph node sampling are standard thoracic surgical procedures. Video-Assisted Thoracic Surgery is now a common-place procedure.

Adjuvant chemotherapy for pathological stage I and II non-small cell carcinoma are gaining acceptance amongst oncologists<sup>1-6</sup>. Randomised trials strongly support the use of three or four cycles of cisplatin-based chemotherapy after complete surgical resection in patients with NSCLC. The benefit observed is in the same range as the improvement obtained with adjuvant chemotherapy in patients with other cancers, such as breast cancer, colon cancer, and ovarian cancer. Selection of patients is important because the chemotherapy does carry toxicity. There is little place for adjuvant radiotherapy for stage I and II lung cancers. Using the targeted therapy agents - the tyrosine kinase inhibitors, as adjuvant treatment is not established.

## Treatment for stage III NSCLC

'Dry' (no pleural effusion) stage III NSCLC are mostly treated with chemotherapy and radiotherapy. Chemotherapy concurrent with thoracic radiotherapy produce the best therapeutic results when compared to the two modalities in sequence. Platinum-based chemotherapy is used. Advance in radiotherapy (3 dimensional radiotherapy, intensity-modulated radiotherapy) enables a high dose of radiation to be delivered more accurately to the target (primary and nodes), and at the same time minimise the dose to critical structures like the spinal cord and the oesophagus. This has improved the outcome i.e. better tumour control with less toxicity, with radiation



therapy to the thorax. Dose-escalating protocols are being worked out, in an attempt to further improve the efficacy.

Other feasible treatments for 'dry' stage III NSCLC include neoadjuvant chemotherapy followed by surgery. This is more of a research topic than everyday practice. Sometimes salvage surgery after definitive chemoradiation is used for residual tumours after chemoradiation.

'Wet' stage III NSCLC (presence of pleural effusion) is usually treated with chemotherapy alone. It is treated more like a stage IV cancer.

### Treatment of stage IV NSCLC

For patients in reasonable performance status (PS<2), chemotherapy doublets with platinum as base, is frequently used. Paclitaxel, gemcitabine, vinorelbine and docetaxel are all useful agents of similar efficacy when combined with either cisplatin or paraplatin. These 'modern' combinations of chemotherapy have a lower toxicity profile than 'older' combinations. Adding the vascular endothelial growth factor (VEGF) inhibitor bevacizumab was reported to have an advantage in outcome compared to chemotherapy alone.

For patients in less favourable performance status, single agents using these chemotherapy agents are still useful for palliation. These can be given at weekly intervals with even less toxicity.

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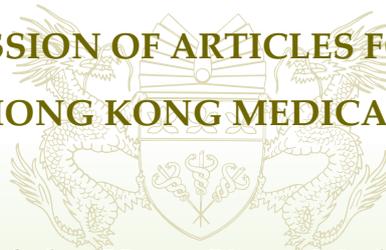
### Treatment for Relapse / Progression

Biological therapy / targeted therapy aiming at epidermal growth factor receptors (EGFR) becomes viable options for second-line treatment after failing first-line chemotherapy. Erlotinib and Gefitinib are similar tyrosine-kinase inhibitors for non-small cell lung cancers. Useful predictors of response include: female, never-smokers, adenocarcinomas and ethnic Asian. Other biologicals are already in the pipeline to be tested in NSCLC.

#### References

1. Arriagada R, et al. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. *N Engl J Med.* 2004;350(4):351-60.
2. Winton T, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. *N Engl J Med.* 2005 Jun 23;352(25):2589-97
3. Douillard JY, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIa non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a randomised controlled trial. *Lancet Oncol.* 2006 Sep;7(9):719-27. Erratum in: *Lancet Oncol.* 2006 Oct;7(10):797.
4. Keller SM, et al. A randomized trial of postoperative adjuvant therapy in patients with completely resected stage II or IIIa non-small-cell lung cancer. Eastern Cooperative Oncology Group. *N Engl J Med.* 2000 Oct 26;343(17):1217-22.
5. Scagliotti GV, et al. Randomized study of adjuvant chemotherapy for completely resected stage I, II, or IIIa non-small-cell lung cancer. *J Natl Cancer Inst.* 2003 Oct 1;95(19):1453-61.
6. Nakagawa M, et al. A randomized phase III trial of adjuvant chemotherapy with UFT for completely resected pathological stage I non-small-cell lung cancer: the West Japan Study Group for Lung Cancer Surgery (WJSG)—the 4th study.

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