New Developments in the Management of Lung Cancer

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Dr Marcus Kennedy
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The Rapid Access Lung Cancer Service
Regional Cancer Centre at CUH
New Developments in the Management of Lung Cancer

• Local developments – CUH RALC and MDT

• Screening for lung cancer – where are we?

• Cases - Deirdre Fitzgerald
  Solitary pulmonary nodules and early stage cancers
  Haemoptysis – the critical symptom
  Worrying symptoms
  Atypical presentations of lung cancer

• New treatment options
  Personalised chemotherapy for lung cancer

• Interventional bronchoscopy – Marcus Kennedy
Lung Cancer in Ireland Stats

- Lung cancer is the leading cause of cancer mortality in Ireland representing approximately 20% of all deaths due to cancer.

- In women - 16.5% of cancer deaths.

- In men - Most common cause of cancer death 24.4% of cancer deaths

Cancer Deaths by Type 2007

<table>
<thead>
<tr>
<th>Type</th>
<th>MALE</th>
<th>FEMALE</th>
<th>ALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>4226</td>
<td>3691</td>
<td>7917</td>
</tr>
<tr>
<td>LUNG</td>
<td>1014</td>
<td>647</td>
<td>1661</td>
</tr>
<tr>
<td></td>
<td>(615 2004)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BREAST</td>
<td>3</td>
<td>611</td>
<td>614</td>
</tr>
<tr>
<td></td>
<td>(663 2004)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROSTATE</td>
<td>550</td>
<td>0</td>
<td>550</td>
</tr>
<tr>
<td>COLORECTAL</td>
<td>558</td>
<td>400</td>
<td>958</td>
</tr>
</tbody>
</table>

Lung cancer kills more Irish people every year than breast and colon cancer combined.
Lung Cancer

• Worldwide numbers are worse

• 1 – 2 million people die each year
  – Projected to be 10 million by 2030

• Full consequences of the tobacco epidemic are yet to come
  – 350 million smokers in China
Patient Identification

- Resectable lung cancer will seldom be diagnosed based on history or physical
- 50% will have evidence of unresectability at the time of first diagnosis
- Further testing reveals another 15%
- 5 - 10% will be found unresectable at surgery
- Therefore, only 25 - 30% are resectable and therefore potentially curable
Screening for Lung Cancer

Where are we?
CXR screening for lung cancer
Lung cancer mortality in the three trials

Routine chest X rays in smokers bring forward the diagnosis of lung cancer but they do not prevent or delay death

<table>
<thead>
<tr>
<th></th>
<th>No (rate) of lung cancer deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>screened control</td>
</tr>
<tr>
<td><strong>London</strong></td>
<td>86 (0.3%) 72 (0.3%)</td>
</tr>
<tr>
<td><strong>Prague</strong></td>
<td>64 (2.0%) 47 (1.5%)</td>
</tr>
<tr>
<td><strong>Mayo Clinic</strong></td>
<td>80 (1.7%) 72 (1.6%)</td>
</tr>
</tbody>
</table>
CT is bound to be a good screening test for lung cancer

Why do a randomised controlled trial with mortality endpoints?

Let’s just start doing it

That’s what they said about chest Xray screening.
Baseline and annual screening of at risk individuals

1.3% detection rate at baseline and 0.3% annual follow up

No control group

? Justification for annual low dose CT in high risk individuals
Figure 2. Combined Results for the Studies of Lung Cancer Screening With Computed Tomography

Should We Screen?

Peter B. Bach; James L. Jett; Ugo Pastorino; et al.


Conducted at the Istituto Tumori (Milan, Italy), the Mayo Clinic (Rochester, Minn), and the Moffitt Cancer Center (Tampa, Fla). The left axis shows the actual and predicted numbers of individuals with different lung cancer outcomes. The right axis shows the number at risk (blue tinted area). P values are for the difference between the observed and the predicted number of events over the course of the study.

http://jama.ama-assn.org/cgi/content/full/297/9/953
Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team

N Engl J Med
Volume 365(5):395-409
August 4, 2011
Results of Three Rounds of Screening.

<table>
<thead>
<tr>
<th>Screening Round</th>
<th>Low-Dose CT</th>
<th>Chest Radiography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total No. Screened</td>
<td>Positive Result</td>
</tr>
<tr>
<td>T0</td>
<td>26,309</td>
<td>7191 (27.3)</td>
</tr>
<tr>
<td>T1</td>
<td>24,715</td>
<td>6901 (27.9)</td>
</tr>
<tr>
<td>T2</td>
<td>24,102</td>
<td>4054 (16.8)</td>
</tr>
</tbody>
</table>

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. Results of screening tests that were technically inadequate (7 in the low-dose CT group and 26 in the radiography group, across the three screening rounds) are not included in this table. A screening test with low-dose CT was considered to be positive if it revealed a nodule at least 4 mm in any diameter or other abnormalities that were suspicious for lung cancer. A screening test with chest radiography was considered to be positive if it revealed a nodule or mass of any size or other abnormalities suspicious for lung cancer.
Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer.

Study Overview

• The National Lung Screening Trial investigators report that persons undergoing three annual screening examinations with low-dose computed tomography had a 20% reduction in lung-cancer mortality as compared with those screened with annual chest radiography.
Lung Cancer in Ireland – Could we do better?

- Currently >75% of patients present with locally advanced or disseminated disease.

- 5-year survival figures for Ireland are only 10% for women. These compare to rates of 16% in France and 18.5% for the United States.
ITS guidelines

• Who should be referred to Rapid Access Clinic?

• Patient with haemoptysis, particularly in a smoker.

• CXR or CT scan suggests lung cancer

www.irishthoracicsociety.com
Background: In recent years around 1,800 people are diagnosed with lung cancer annually – approximately 1,100 men and 700 women. Incidence rates are decreasing for men but increasing for women. Less than 1% of all new cases occur before the age of 40. More than 90% of patients are symptomatic at presentation. Currently over a third of patients have distant metastases by the time of diagnosis.

Risk Factors: Smoking, including passive smoking and smoking marijuana; radon exposure; exposure to heavy metals such as arsenic; radiation; asbestos dust; previous history of cancer (e.g. head & neck cancer). Smoking avoidance/cessation is the most important preventive strategy as over 90% of lung cancer can be attributed to cigarette smoke. However lung cancer can occur in patients without any of the listed risk factors.

ABOUT RAPID ACCESS SERVICES FOR LUNG CANCER

Rapid Access Services provide initial investigations, such as CT and bronchoscopy, to patients with suspected lung cancer, usually within one or two hospital visits. This reduces multiple hospital visits and patient anxiety and shortens the time period to diagnosis.

Patients should be assessed in the lung cancer rapid access service by a respiratory physician within 2 weeks of receipt of request.

Who can refer your patient to the rapid access service?

- you, the GP
- a radiologist (in conjunction with GP)
- another hospital based clinician, e.g. from the Emergency Department

Who should you refer to the Rapid Access Service?

- a patient whose chest x-ray is suspicious of lung cancer.
  Please include details on the referral of the hospital in which the investigation was carried out. If this was a different hospital/clinic, please fax or post a copy of the result to the clinic and request a copy of the film for the patient to bring with them if possible.
- a patient who has haemoptysis, or other symptoms which are concerning or persistent, even if their chest x-ray is normal.

When is referral to the rapid access service not appropriate?

If a patient presents with life threatening symptoms, an emergency referral should be made in the usual manner.

Table 1: Indications for Urgent Chest X-ray

A patient with the following signs or symptoms should be referred for urgent chest x-ray. A report should be back to the GP within one week of request.

**Symptoms**

- Haemoptysis
- New onset unexplained or persistent cough (>3 weeks)
- Alteration in character/severity of chronic cough
- Unexplained chest pain or dyspnoea
- Unexplained weight loss/cachexia
- Unexplained bone pain/neurological symptoms

**Signs**

- Clubbing
- Lymphadenopathy
- Focal chest signs
- Hepatomegaly

Note: if there is a suspicion of lung cancer, it is not advisable to delay referral by ordering an outpatient CT. A rapid access service can arrange both imaging and bronchoscopy.


The guideline represents the view of the NCCE which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of health professionals to make decisions appropriate to each patient. This guideline will be reviewed as new evidence emerges.

Version 1.0 Date: January 2010
Urgent Referral –
Rapid Access Lung Cancer Dec 2010
Fax RALC referral form to 021 4922391
or 021 4920168
FAO Mike Henry / Marcus Kennedy

• 2 dedicated lung cancer specialists
  Mike Henry / Marcus Kennedy
  Secretary Helen – 021 4921069

• 2 dedicated lung cancer nurse specialists
  Sharon Guiry 086 7872199
  Pauline O’Dea 087 9058003
NATIONAL LUNG CANCER RAPID ACCESS SERVICE REFERRAL FORM

POST or FAX this FORM to ONLY ONE of the Lung Cancer Rapid Access Services to avoid duplication. (Please ✓)

- Beaumont Hospital, Dublin 9 Tel: (01) 891 2544 Fax: (01) 779 4689
- Cork University Hospital, Cork Tel: (021) 422 0224 Fax: (021) 422 0224
- Galway University Hospital Tel open in mid 2010
- Mater University Hospital, D.7 Tel: (01) 803 2564;803 2595 Fax: (01) 803 4636
- Mid-Western Regional Hospital, Limerick To open mid 2010
- St. James’s Hospital, Dublin 8 Tel: (01) 410 2549 Fax: (01) 410 2549
- St. Vincent’s University Hospital, Dublin 4 Tel: (01) 221 2162 Fax: (01) 221 2162
- Waterford Regional Hospital, Waterford Tel: (051) 841 988 Fax: (051) 841 844

Patient Details

Surname: ____________________________ First Name: ____________________________ DOB: ____________________________
Address: ____________________________

Mobile No.: ____________________________ Tel: ____________________________
Tel evening: ____________________________
Hospital No. If known: ____________________________
First Language: ____________________________ Interpreter required: Yes ☐ No ☐
Gender: Male ☐ Female ☐ Wheelchair assistance: Yes ☐ No ☐

General Practitioner or Details

Name: ____________________________
Address: ____________________________

Telephone: ____________________________ Mobile: ____________________________
Fax: ____________________________
GP Signature: ____________________________ Date of referral: ____________________________
Medical Council Registration No.: ____________________________

Referral Information

Main indications for referral are an abnormal chest X-ray or haemoptysis.

SYMPTOMS
☐ Haemoptysis
☐ Other persistent unexplained symptoms

SMOKING STATUS
☐ Current smoker ☐ Ex-smoker ☐ Non-smoker

CLINICAL EXAMINATION
☐ Clubbing ☐ Lymphadenopathy ☐ Hypoventilation ☐ Other

Chest X-ray
Date of Chest X-Ray: ____________________________
Hospital: ____________________________
☐ Normal
☐ Abnormal (suggestive of lung cancer)
Please attach/fix copy of result if possible

CT Scan (if done)
Date of CT Scan: ____________________________
Hospital: ____________________________
☐ Normal
☐ Abnormal (suggestive of lung cancer)
Please attach/fix copy of result if possible

Past medical history:
☐ Asthma ☐ Renal Insufficiency
☐ Other details: ____________________________

Allergies: ☐ Yes ☐ No
Details: ____________________________
☐ History of allergy to contrast dye

Anticoagulants: ☐ Yes ☐ No
Details: ____________________________

Medications:

Comments:

Has patient been advised of possible diagnosis of lung cancer? ☐ Yes ☐ No

FOR HOSPITAL USE:

Date of referral received: ____________________________
Date of appointment offered: ____________________________
Reason patient did not accept first appointment offered: ____________________________

Guidelines:
☐ Urgent Referral (to be seen within 2 weeks)
☐ Early Referral (to be seen within 6 weeks)
☐ Routine Referral (to be seen within 12 weeks)

Lung Clinic Triggers

Triggers by: ____________________________

Version 1.0 January 2010
RALC clinic – Monday am

• Mike Henry or Marcus Kennedy + SpR
• KPI – patients must be seen within 10 working days of referral
• CT in advance of clinic
• Lung cancer CNS – spirometry and information.
• Approx 30% referrals have cancer.
• Follow up patients post radical therapy for 5 years
• Virtual SPN clinic
RALC clinic – Monday am

- We often defer decision on next test until the following days MDT
- If palpable supraclavicular node – cytopath FNA – usually same day results – Dr Julie McCarthy
- If pleural effusion ultrasound guided tap – cytopath – usually same day results.
- Patient spends some time with CNS – information given
- Smoking cessation advice
In total there were 254 patients diagnosed with a new primary lung cancer at MDM in 2011 at CUH.

92 of those diagnosed at MDM during 2011 came from the RALC. A further 85 patients came from other referral sources at CUH (e.g. inpatient referrals, incidental radiological findings, A&E referrals etc.) and the other 77 were referred from other hospitals.
KPI Clinic  Access 2012
Jan - Jun

There has been an increase of 33% in clinic attendances in 2012 in comparison to 2011 and this has affected our Access KPI.
Surgical resection rates in CUH

- 42 patients had a surgical resection for primary lung cancer in the first 6 months of 2012.

- This is an increase of 75% in comparison with 2011 when 24 patients had surgery during the same period.
Case 1 – T O’R

- 78 year old male, asymptomatic
- Ex-smoker > 60 years
- Attended GP for check up
- Noted to have right basal crackles + sent for CXR
- Nodule on CXR
- Referred to RALC
CT Thorax
• Discussed at Lung MDT
  – Spirometry: FEV1 2.83L
  – ECOG: 0

• Booked for PET + CT – guided biopsy
PET
Management

• Stage 1b lung cancer
  – T2N0M0 by PET staging

• Referred for surgical opinion + reviewed this week
  – For VATS excision, frozen section +/- right lower lobectomy.
Indeterminate SPN

4-8 mm*
- F/U CT (volumetrics) 6-12/24 mo.

Highly suspicious for CA
- Biopsy/resect

>8 mm
- Contrast CT/PET/Bx
- Solid
- F/U 6/12/24

* nodules < 4 mm = no followup (non-high-risk patient)
Lung Nodule Follow Up

- Fleischner Society Guidelines

<table>
<thead>
<tr>
<th>Nodule Size (mm)*</th>
<th>Low-Risk Patient†</th>
<th>High-Risk Patient‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4</td>
<td>No follow-up needed§</td>
<td>Follow-up CT at 12 mo; if unchanged, no further follow-up¶</td>
</tr>
<tr>
<td>&gt;4–6</td>
<td>Follow-up CT at 12 mo; if unchanged, no further follow-up¶</td>
<td>Initial follow-up CT at 6–12 mo then at 18–24 mo if no change ‖</td>
</tr>
<tr>
<td>&gt;6–8</td>
<td>Initial follow-up CT at 6–12 mo then at 18–24 mo if no change</td>
<td>Initial follow-up CT at 3–6 mo then at 9–12 and 24 mo if no change</td>
</tr>
<tr>
<td>&gt;8</td>
<td>Follow-up CT at around 3, 9, and 24 mo, dynamic contrast-enhanced CT, PET, and/or biopsy</td>
<td>Same as for low-risk patient</td>
</tr>
</tbody>
</table>

Note.—Newly detected indeterminate nodule in persons 35 years of age or older.
* Average of length and width.
† Minimal or absent history of smoking and of other known risk factors.
‡ History of smoking or of other known risk factors.
§ The risk of malignancy in this category (<1%) is substantially less than that in a baseline CT scan of an asymptomatic smoker.
¶ Nonsolid (ground-glass) or partly solid nodules may require longer follow-up to exclude indolent adenocarcinoma.

Case 2 – RE
How do you investigate the mediastinum

- 71 year old male
- Presented to GP with persistent cough and dyspnoea, retrosternal discomfort
- Current heavy smoker, 50 pack year hx
- OGD - Normal
CT of the Mediastinum

Operator Characteristics

- \( N = 4,793 \)
- Sensitivity = \( .60 (.51-.68) \)
- Specificity = \( .81 (.74-.86) \)
- That means an enlarged lymph node has a 20% chance of not having cancer within it.
- Conversely, a CT scan of the chest that has no evidence of adenopathy will harbor tumor at surgery up to 32-49% of the time.
Operator Characteristics

- N = 1,111 nodal stations
- Sensitivity = .85 (.79-.89)
- Specificity = .88 (.82-.92)
- That means a hot lymph node on PET has a 8-18% chance of not having cancer within it.
- Conversely, a negative PET will harbor tumor at surgery up to 11-21% of the time.
Blind (TBNA)

- TBNA in NSCLC, meta analysis
  - Yield 39-78%

Holty J et al, Thorax 2005 - meta analysis -
Evolving staging strategies

CT + MS:

CT + PET + E(B)US + (MS):

CT/PET + E(B)US + (MS):
EBUS
## Invasive mediastinal staging of lung cancer

<table>
<thead>
<tr>
<th></th>
<th>Patients N0</th>
<th>Sensitivity %</th>
<th>FP %</th>
<th>FN %</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediastinoscopy</td>
<td>6505</td>
<td>78%</td>
<td>0%</td>
<td>11%</td>
<td>39%</td>
</tr>
<tr>
<td>EBUS-NA</td>
<td>918</td>
<td>90%</td>
<td>0%</td>
<td>20%</td>
<td>68%</td>
</tr>
<tr>
<td>EUS-NA</td>
<td>1003</td>
<td>84%</td>
<td>0.7%</td>
<td>19%</td>
<td>61%</td>
</tr>
</tbody>
</table>

Detterbeck et al., Chest 2007;132:202S-220S
• Provide access to different areas of the mediastinum

• In combination most mediastinal LNs can be sampled

• In four series the accuracy of EUS-FNA and EBUS-TBNA in combination for the diagnosis of mediastinal cancer was 95%

Herth et al., AJRCCM, 2005; Rintoul et al., Eur Respir J, 2005; Vilman et al., Endoscopy, 2006; Wallace et al., JAMA 2008
Benefits

- Low risk procedure
- Day case
- Comparable sensitivity
  - If not better
- Cost benefit
- On site cytology

EBUS – AND ROSE

EBUS TBNA – same day diagnosis and staging

85% success rate in CUH only
Case - Atypical Presentation

• 67 year old male
• Heavy smoker
• Admitted for ix of proteinuria
  – Membranous Glomerulonephritis on renal bx
• CXR on admission

Pleural fluid negative for malignancy

CT guided biopsy confirmed squamous cell carcinoma
PET

Confirmed locally invasive disease
Stage IIIa on radiology
Management

• Left upper lobectomy
• Discharged well last week
<table>
<thead>
<tr>
<th>T and M</th>
<th>6th edition TNM</th>
<th>7th edition TNM</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (&lt;3 cm)</td>
<td>T1a (≤ 2 cm)</td>
<td>IA</td>
<td>IIA</td>
<td>IIIA</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T1b (&gt;2–3 cm)</td>
<td>IA</td>
<td>IIA</td>
<td>IIIA</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td>T2 (&gt;3 cm)</td>
<td>T2a (&gt;3–5 cm)</td>
<td>IB</td>
<td>IIA (IB)</td>
<td>IIIA</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T2b (&gt;5–7 cm)</td>
<td>IIA (IB)</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T3 (&gt;7 cm)</td>
<td>IIB (IB)</td>
<td>IIIA (IB)</td>
<td>IIIA</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td>T3 invasion</td>
<td>T3</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIA</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td>T4 (same lobe nodules)</td>
<td>T3</td>
<td>IIIB</td>
<td>IIIA (ⅢB)</td>
<td>IIIA (ⅢB)</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td>T4 (extension)</td>
<td>T4</td>
<td>IIIA (ⅢB)</td>
<td>IIIA (ⅢB)</td>
<td>IIIB</td>
<td>IIIB</td>
<td></td>
</tr>
<tr>
<td>M1 (ipsilateral lung)</td>
<td>T4</td>
<td>IIIA (Ⅳ)</td>
<td>IIIA (Ⅳ)</td>
<td>IIIB (Ⅳ)</td>
<td>IIIB (Ⅳ)</td>
<td></td>
</tr>
<tr>
<td>T4 (pleural effusion)</td>
<td>M1a</td>
<td>IV (ⅢB)</td>
<td>IV (ⅢB)</td>
<td>IV (ⅢB)</td>
<td>IV (ⅢB)</td>
<td></td>
</tr>
<tr>
<td>M1 (contralateral lung)</td>
<td>M1a</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>M1 (distant)</td>
<td>M1b</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td></td>
</tr>
</tbody>
</table>

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Change in classification with 7th edition of TNM from 6th edition in ( )
BTS guidelines

• Radical surgery for up to Stg IIIa tumours
  – Includes T4, N0-1.

• Surgery for N2 disease can be considered if non fixed, non bulky, localised nodes.

• Lung preserving surgery:
  – Wedge resection for small lesions
  – Sleeve lobectomy instead of pneumonectomy
Sleeve lobectomy

Case 4 – MO’S

- 64 year old female
- Never smoker
- Presented with haemoptysis
- Locally advanced disease
- Diagnosed with Stage IIIa adenocarcinoma

Non smoking female adenocarcinoma
Tested for EGFR status – positive
• Started on erlotinib 150mg bd
  – EGFR TKI
• Maximal therapy achieved Feb 2012
• Combined chemotherapy with a view to further tumour shrinkage to allow for radiotherapy (cisplatin and pemetrexed)

• Initial response but progression of disease on follow up CXR

• Referred for palliative care June 2012
Gefitinib or Carboplatin–Paclitaxel in Pulmonary Adenocarcinoma

Tony S. Mok, M.D., Yi-Long Wu, M.D., F.A.C.S., Sumitra Thongprasert, M.D., Chih-Hsin Yang, M.D., Ph.D., Da-Tong Chu, M.D., Nagahiro Saijo, M.D., Ph.D., Patrapim Sunpaweravong, M.D., Baohui Han, M.D., Benjamin Margono, M.D., Ph.D., F.C.C.P., Yukito Ichinose, M.D., Yutaka Nishiwaki, M.D., Ph.D., Yuichiro Ohe, M.D., Ph.D., Jin-Ji Yang, M.D., Busyamas Chewaskulyong, M.D., Haiyi Jiang, M.D., Emma L. Duffield, M.Sc., Claire L. Watkins, M.Sc., Alison A. Armour, F.R.C.R., and Masahiro Fukuoka, M.D., Ph.D.

**B EGFR-Mutation–Positive**
- Hazard ratio, 0.48 (95% CI, 0.36–0.64) P<0.001
- Events: gefitinib, 97 (73.5%); carboplatin plus paclitaxel, 111 (86.0%)

**C EGFR-Mutation–Negative**
- Hazard ratio, 2.85 (95% CI, 2.05–3.98) P<0.001
- Events: gefitinib, 88 (96.7%); carboplatin plus paclitaxel, 70 (82.4%)

P Interaction (comparing HRs 0.48 vs. 2.85): <0.001

Tailored Chemotherapy

- Genetic mutations associated with tumour growth and metastases
- Numerous genes identified
- Targets at present include:
  - EGFR (Erlotinib)
  - ALK (Crizotinib)
  - KRAS – resistance to TKI

Molecular Classification of Adenocarcinoma

Western (Adeno)

East Asian

Comprehensive genetic profiling of 500 each of lung squamous and adeno carcinomas