Genotype testing and targeted therapy in lung cancer: Success and limitations in implementing a scientific advance

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Lung cancer in New Zealand

➢ One of the most common cancers
  • 9% of all new cancer registrations (~2000 cases per year)
  • Non-squamous non-small cell lung cancer (NSCLC) is the most common subtype (~60% of all lung cancer cases).

➢ Leading cause of cancer mortality
  • ~18% of all cancer deaths (~1650 deaths per year)
  • One-year survival = ~30%
  • Five-year survival = ~11%
    (Māori: 6.5%; non-Māori: 11.9%)
    (Most deprived: 9.7%; least deprived: 13.0%)

EGFR targeted therapy

- Epidermal Growth Factor Receptor (EGFR) is a common oncogenic driver in non-squamous NSCLC.
- EGFR Tyrosine Kinase Inhibitors (TKIs) block downstream signalling pathways, and have been shown to improve progression-free survival.
Population-based cohort study in Northern NZ

- Involved all patients diagnosed with non-squamous NSCLC in four DHBs between 2010 and 2015.
- Data sources: NZ Cancer Registry, TestSafe, laboratory, pharmaceutical and medical records.
- 2701 eligible patients identified:
  - 51% - females
  - 17% - Māori; 10% - Pacific; 10% - Asian
  - 62% - adenocarcinoma
  - 52% - diagnosed with distant metastasis
  - 19% - diagnosed based on clinical investigation only
## Testing prevalence
- 39.2% were tested for EGFR mutation(s).
- Higher testing prevalence in:
  - younger patients, females, Asians
  - patients with adenocarcinoma or local spread
  - patients from less deprived neighbourhoods
  - Patients from Waitemata DHB
- Very low testing prevalence (3%) in patients diagnosed based on clinical investigation only (i.e., no available tissue for testing).

## Mutation prevalence
- Of the tested patients, 21.6% were mutation positive.
- Higher mutation prevalence in:
  - Females, Asians, non-smokers
  - Patients with adenocarcinoma
Time trends in testing prevalence, patient selection & mutation prevalence

- Testing prevalence increased after the commencement of routine testing.
- Patient selection decreased.
- Testing uptake was consistently low in:
  - patients aged over 80 years
  - Māori patients
  - patients diagnosed based on clinical investigation only

- Mutation prevalence decreased with increase in testing prevalence and decrease in patient selection.
- Mutation prevalence could be as low as 15.5% if all patients were tested.
- At least 11.5% of untested patients could be mutation positive.

Tin Tin et al. *Cancer Epidemiology* 2018;57:24-32
Impact of EGFR mutation testing

EGFR mutation testing improves patient survival, appropriate drug prescribing and response to EGFR-TKI treatment.

McKeage et al. Targeted Oncology 2017;12(5):663-75
**Summary**

<table>
<thead>
<tr>
<th><strong>Success</strong></th>
<th><strong>Limitations</strong></th>
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<tbody>
<tr>
<td>The uptake of EGFR mutation testing has improved over time.</td>
<td>EGFR mutation testing is still suboptimal:</td>
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<tr>
<td>EGFR mutation testing has improved:</td>
<td>• Only two-thirds were tested in 2015.</td>
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<td>• appropriate drug prescribing</td>
<td>• Testing was low in Māori and 80+ year old patients.</td>
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<td>• response to treatment</td>
<td>• Full uptake of testing was limited by a lack of availability of specimens for testing and variable testing referral practices.</td>
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<td>• survival</td>
<td><strong>Incomplete testing uptake has important implications:</strong></td>
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<td>• The mutation prevalence observed may not be accurate.</td>
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<tr>
<td></td>
<td>• Untested patients may not be treated appropriately.</td>
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