BC Cancer Agency Centres
Lung Cancer – Diagnosis and Therapy update

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Disclosure

• Advisory board: Astra-Zeneca, Merck
• Honorarium: Merck, Janssen, Astra-Zeneca
Learning objectives

• By the end of this session, participants will be able to:

1) Describe the roles of various therapies for lung cancer;

2) State the indications for surgical, radiation and immunotherapies; and

3) Discuss the management of side-effects from these therapies.
Still #1 killer

• Most common cause of cancer related mortality in men and women in Canada
• 26,000 new diagnoses/year
• 27% of all cancer deaths
• 10-15% non-smoker (?)

Canadian Cancer Society 2015
Survival

![Bar chart showing survival rates by stage at diagnosis.]

- Stage I: 1 year survival = 71.12%, 5 year survival = 35.33%
- Stage II: 1 year survival = 48.15%, 5 year survival = 20.89%
- Stage III: 1 year survival = 34.59%, 5 year survival = 6.32%
- Stage IV: 1 year survival = 14.36%
- Stage Not Known: 1 year survival = 16.61%, 5 year survival = 5.79%
- All Stages: 1 year survival = 32.16%, 5 year survival = 9.68%
Survival

Non-Small Cell Lung Cancer Survival Rate
Patients Diagnosed with Distant (Metastatic) Cancer Between 2000-2011
Cancer Treatment Centers of America

<table>
<thead>
<tr>
<th>Years (after initial diagnosis)</th>
<th>Patient Survival Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>65</td>
</tr>
<tr>
<td>1</td>
<td>44</td>
</tr>
<tr>
<td>1.5</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>2.5</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
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<tr>
<td>3.5</td>
<td>9</td>
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<tr>
<td>4</td>
<td>7</td>
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<tr>
<td>4.5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>
What can we improve?

• Lung cancer screening
• Speedy diagnostic workup
• More effective treatment
• Better and earlier palliative care
Trivia

• What are the types of lung cancer?

• Answer: small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC)
Types of lung cancer

- Adenocarcinoma
- Small-cell carcinoma
- Non-smoker
- Squamous cell carcinoma
- Other or unspecified
- Non-smoker
- Smoker
- Large cell carcinoma

- Smoker
- Non-smoker
Trivia

• What are the stages of lung cancer?

• Answer: I, II, III, IV
Trivia

• What are the TNM stages for stage III lung cancer?

• Answer
  - All N2 and N3 diseases
  - N≥1 + T3
  - All T4 diseases
Lymph nodes

Supraclavicular zone
- 1 Low cervical, supraclavicular, and sternal notch nodes

Superior Mediastinal Nodes
- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Pre-vascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

Aortic Nodes
- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)

Regional Lymph Nodes (N)
- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastases
- N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
- N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
- N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
Lymph nodes
Staging

• Practical tips for consultation
  - Accurate assessment of functional status, comorbidities (esp cardiorespiratory) and geriatric evaluation
  - Patient situation (financial, work, health insurance, smoking status, support)
  - Plan investigations ahead of time
    - Always ensure CT contrast or MR of head, PFT, PET, BW including LFTs, proper lymph node staging have been done
Staging

CT contrast or MR head

PFT

Biopsy
Mediastinal LN

PET
BW, LFTs
Small cell lung cancer

• Generally a systemic disease
• Very responsive to chemotherapy, but also very aggressive
• Platinum + etoposide x 4-6 cycles with concurrent radiation to chest followed by PCI if limited stage
• Platinum + etoposide x 4-6 cycles followed by PCI (+/- sequential chest radiation) if extensive stage
• Generally treated very urgently
Non-small cell lung cancer
Case 1

- 80F, 50PY smoking history, quit 10y ago
- DM, CAD (stent 10 years ago), OA
- Uses walker
- Lives alone with support from daughter
- Due to cough, x-ray done then CT to follow-up
- FEV1 = 55% of predicted
Case 1
Case 1

- Independent predictors of major adverse outcomes after pneumonectomy
  - Age 65 years or older (p < 0.001)
  - Male sex (p = 0.026)
  - Congestive heart failure (p = 0.04)
  - Forced expiratory volume in 1 second less than 60% of predicted (p = 0.01)
  - Benign lung disease (p = 0.006)
  - Requiring extrapleural pneumonectomy (p = 0.018).
  - Those receiving neoadjuvant chemoradiotherapy were more at risk for major morbidity than patients without induction therapy (p = 0.049).

Grade 3 events 30-35%, mortality 5-6%

Shapiro Ann Thorac Surg. 2010
Case 1

- Predictors of prolonged length of stay after lobectomy
  - Age per 10 years (odds ratio [OR], 1.30, p < 0.001)
  - Zubrod score (OR, 1.51; p < 0.001)
  - Male sex (OR, 1.45; p = 0.002)
  - American Society of Anesthesiology score (OR, 1.54; p < 0.001)
  - Insulin-dependent diabetes (OR, 1.71; p = 0.037)
  - Renal dysfunction (OR, 1.79; p = 0.004), induction therapy (OR, 1.65; p = 0.001)
  - Percentage predicted forced expiratory volume in 1 second in 10% increments (OR, 0.88; p < 0.001)
  - Smoking (OR, 1.33; p = 0.095)

Grade ¾ event 25%; Mortality 1-2%  
Cao ACS 2012
Case 1

- PPO FEV1 = preoperative FEV1 x (1 – y/z) where y = number of functional or unobstructed lung segments to be removed, and z = total number of functional segments (typically 19)

- Similar formula for PPO DLCO
  - If both >60%, surgery is a go
  - If one of them <30%, additional exercise testing
  - If both <30%, no go
Case 1

• **Wedge resection/segmentectomy**
  - In 1 prospective study (Lung Cancer Study Group trial 801), increased rate of local recurrence (5.4 versus 1.9 percent) and trend toward worse survival for limited resection vs. lobectomy (stage IA)
  - In large retrospective studies, worse survival/outcome for wedge resection
  - Single institutional series/elderly patients: similar
  - 2014 meta-analysis: If lesion <2cm, probably similar
  - Ongoing clinical trials: Cancer and Leukemia Group B (CALGB) trial 140503 (NCT00499330) and the Japan Clinical Oncology Group (JCOG) 0802/WJOG 4607L 1000

Ginsberg Ann Thorac Surg 1995
Case 1

Table 1
Current common Canadian indications for lung, liver and spine stereotactic body radiotherapy and the total doses/number of fractions prescribed

<table>
<thead>
<tr>
<th>Lung</th>
<th>Liver</th>
<th>Spine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medically inoperable T1/T2</td>
<td>60 Gy/8 fractions</td>
<td>Previously irradiated spine metastases</td>
</tr>
<tr>
<td>N0M0 non-small cell lung cancer</td>
<td>50 Gy/5 fractions</td>
<td>35 Gy/5 fractions</td>
</tr>
<tr>
<td>Lung metastases</td>
<td>48 Gy/4 fractions</td>
<td>Spine metastases with no prior radiation</td>
</tr>
<tr>
<td>Tumours less than 5 cm</td>
<td>54–60 Gy/3 fractions</td>
<td>24–26 Gy/3 fractions</td>
</tr>
<tr>
<td></td>
<td>34 Gy/1 fraction</td>
<td>Postoperative patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(± prior radiation exposure)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Selected primary spinal tumours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No more than three consecutive vertebrae</td>
</tr>
</tbody>
</table>

5Y local recurrence 7%
5Y locoregional recurrence 38%
5Y distant recurrence 15%
Case 1

• Exclusion for SBRT (per RTOG 0236)
  - Patients with T2 or T3 primary tumors > 5 cm or patients with T3 primary tumors involving the central chest and structures of the mediastinum
  - The primary tumor of any T-stage within or touching the zone of the proximal bronchial tree defined as a volume 2 cm in all directions around the proximal bronchial tree (carina, right and left main bronchi, right and left upper lobe bronchi, intermedius bronchus, right middle lobe bronchus, lingular bronchus, right and left lower lobe bronchi)

Timmerman JAMA 2010
Case 1

Zone of proximal bronchial tree, the “No Fly Zone”, as defined in RTOG 0236 protocol.
Case 1

- **Surgery vs. SBRT**
  - ???????
  - STAR/ROSEL trials combined analysis
  - <4cm N0 lesions, n=58
  - 3YS 95% (95% CI 85–100) in the SABR group compared with 79% (64–97) in the surgery group (hazard ratio [HR] 0·14 [95% CI 0·017–1·190], log-rank p=0·037)
  - 3Y RFS 86% (95% CI 74–100) in the SABR group and 80% (65–97) in the surgery group (HR 0·69 [95% CI 0·21–2·29], log-rank p=0·54)
  - Ongoing clinical trials
Case 1

- Received SBRT over 2 weeks
- Tolerated very well with grade 1 fatigue only
Case 1

• Follow-up – unclear evidence for benefit
  - In retrospective studies, no difference
  - In 1 prospective study, CXR Q3m + bronch/CT Q6m --> of 136 with recurrence, 85 were diagnosed by a scheduled procedure, 36 of whom were asymptomatic. More than twice as many thoracic recurrences documented by a scheduled test were eligible for potentially curative resection (22 of 85 versus 6 of 51 [26 versus 12 %]).
  - Alberta: CXR/HP Q3m x 2 years then Q3m x 3 years + CT Q6m x 2 years then low dose CT Q1y x 3 years
  - BC guideline says “no evidence for routine scan” (?)

<table>
<thead>
<tr>
<th>On P</th>
<th>Norm</th>
<th>Health</th>
<th>Incidental</th>
<th>Light</th>
<th>55M</th>
</tr>
</thead>
</table>

- **Case 2**
- 55M
- Light smoker
- 20Y, quit 10 years ago
- Incidental finding of 3cm lesion
- Healthy, no comorbidities
- Normal lung function on PFT
- On PET, N1 disease

http://staginglungcancer.org/stages/IIA-T2aN1
Case 2

- Surgery!
- T2aN1 = IIA

http://staginglungcancer.org/
Case 2
Case 2

- 4 weeks later...
  - Pre-op PET and CT head normal
  - Brief a.fib post-op but no significant morbidity
  - Recovered well otherwise
  - Normal lab other than slight anemia
  - Pathology report: pT2a (3.2cm) N1 (1/5 LN involved) moderately differentiated squamous cell carcinoma, 2 mediastinal LN resected
Case 2

- Adjuvant chemotherapy?
  - Yes!
  - 5% survival benefit in 5 years
  - Need significant supportive care
  - Standard regimen vinorelbine/cisplatin
  - Carboplatin/paclitaxel – easier, but evidence of benefit less clear
Case 2

• How good should lymph node dissection be?
  - Meta-analysis: dissection of levels 4, 7, and 10 for right sided lesions, and levels 5 or 6 and 7 for left sided lesions, improved survival (HR 0.78)
  - Sampling vs dissection (Z0030): sampling of 2R, 4R, 7, and 10R for right-sided tumors and 5, 6, 7, and 10L for left-sided tumors; if all negative, dissection = no dissection in outcome (unexpected N2 + only 3.8%)

Case 2

NCI-Canada BR.10 Study of Adjuvant Chemotherapy vs. Observation Alone: Schema

T1-2, N0-1 NSCLC
N2 nodes sampled
N = 482
Stratified by:
N0 vs N1
Ras pos, neg, unknown

Cisplatin 50 mg/m² d1, 8
Vinorelbine 30 → 25 mg/m²/wk x 4

No chemotherapy

0.8% died, 58% completed 3 or more cycles,
77 percent had at least one dose reduction or omission, and 55 percent required one dose delay or more

Winton, NEJM 352:2582, 2005
Case 2

Table 1 Adjuvant chemotherapy of completely resected NSCLC

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Stage</th>
<th>Chemo</th>
<th>5-year survival (%)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chemo</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>ALPI-EORTC</td>
<td>1,088</td>
<td>I-IIIA</td>
<td>MVP</td>
<td>49.0</td>
<td>48.0</td>
<td>0.96 (0.81-1.13)</td>
</tr>
<tr>
<td>IALT</td>
<td>1,867</td>
<td>I-III</td>
<td>Cis/Vinca</td>
<td>44.5</td>
<td>40.4</td>
<td>0.86 (0.76-0.98)</td>
</tr>
<tr>
<td>JBR.10</td>
<td>482</td>
<td>IB-II</td>
<td>Cis/Vino</td>
<td>69.0</td>
<td>54.0</td>
<td>0.69 (0.52-0.91)</td>
</tr>
<tr>
<td>ANITA</td>
<td>840</td>
<td>IB-IIA</td>
<td>Cis/Vino</td>
<td>51.2</td>
<td>42.6</td>
<td>0.80 (0.66-0.96)</td>
</tr>
<tr>
<td>CALGB</td>
<td>344</td>
<td>IB</td>
<td>Carbo/Pacl</td>
<td>57.0</td>
<td>59.0</td>
<td>0.80 (0.60-1.07)</td>
</tr>
<tr>
<td>BLT</td>
<td>381</td>
<td>I-III</td>
<td>Cis-based</td>
<td>NR</td>
<td>NR</td>
<td>1.0</td>
</tr>
<tr>
<td>LACE meta-analysis</td>
<td>4,584</td>
<td>I-IIIA</td>
<td>Cis-based</td>
<td>48.8</td>
<td>43.5</td>
<td>0.89 (0.82-0.96)</td>
</tr>
</tbody>
</table>

NR, not reported; NS, not significant; NSCLC, non-small cell lung cancer.

- Across the studies,
  - No predictive biomarker (e.g. ERCC1, KRAS etc)
  - Magnitude of benefit ~ 5-10%
  - Tumour has to be at least 4cm or larger if N0, or at least N1
Case 2

• PORT?
  - Generally no (increases harm)
  - 2 cases in which PORT can be considered:
    ➢ Positive margin
    ➢ Resected N2 disease

Case 2

• BR. 31
  - 2:1 randomization to durvalumab Q4w x 1 year vs. placebo Q4w x 1 year
  - Can be post adjuvant chemo or patients who refused chemo after surgery
  - Open at BCCA sites
Case 3

• 72M
• Current smoker
• FEV1 70%
• Frail looking, but well supported by wife
• No significant comorbidities, but has not gone to the doctor until recently
• CT head negative, lab reasonable
Case 3

Large left lung primary and periaortic ipsilateral LN
T2b N2 = IIIA
Case 3

• Biopsy revealed poorly differentiated adenocarcinoma from the main tumour.
• Mediastinal LN not accessed due to technical difficulties
Case 3

• RT/chemo vs RT trials
  - Shows approximately 5-10% 5Y survival benefit by adding chemotherapy in various trials (Furuse JCO 1999, CALGB8433, Intergroup ECOG 5488/RTOG 8808/CALGB 8433, Schaake-Koning NEJM 1992)
  - Meta-analysis
    - Pritchard 1999: HR 0.87 at 2 years, 0.83 at 3 years for adding chemo (concurrent or sequential) in 14 trials
    - Auperin 2006: absolute benefit of RT/chemo vs chemo 4% at 2 years in 6 trials
    - Le Chevalier 2007: absolute benefit of RT/chemo vs RT → chemo 2.2% at 5 years
Case 3

- Trimodality trials

<table>
<thead>
<tr>
<th>Study/Reference</th>
<th>No. of Patients</th>
<th>Stage IIIIB (%)</th>
<th>N3/T4 (%)</th>
<th>Chemotherapy</th>
<th>Radiotherapy</th>
<th>Complete Resection (%)*</th>
<th>Operative Mortality (%)</th>
<th>Median Survival (months)</th>
<th>95% CI (months)</th>
<th>5-Year Survival (95% CI (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany²</td>
<td>264</td>
<td>69</td>
<td>22/62</td>
<td>P, E</td>
<td>45 Gy + C, Vin</td>
<td>37</td>
<td>9</td>
<td>16</td>
<td>13 to 18</td>
<td>3 yr: 28  22 to 33</td>
</tr>
<tr>
<td>Esson, Germany (retrospective series, operated patients)²</td>
<td>392</td>
<td>44</td>
<td>NR</td>
<td>P, E or C, T</td>
<td>45 Gy bid + P, E</td>
<td>NR</td>
<td>5</td>
<td>22</td>
<td>NR</td>
<td>IIIA: 5 yr: 36 IIIB: 5 yr: 28</td>
</tr>
<tr>
<td>SWOG8805, United States (subgroup)³</td>
<td>51</td>
<td>100</td>
<td>53/47</td>
<td>P, E</td>
<td>45 Gy</td>
<td>63</td>
<td>10</td>
<td>17</td>
<td>NR</td>
<td>3 yr: 24</td>
</tr>
<tr>
<td>IGR, France⁵</td>
<td>40</td>
<td>100</td>
<td>45/75</td>
<td>P, F, Vbl</td>
<td>42 Gy</td>
<td>58</td>
<td>7</td>
<td>14⁺</td>
<td>NR</td>
<td>19  10 to 34</td>
</tr>
<tr>
<td>Rome, Italy⁵</td>
<td>39</td>
<td>100</td>
<td>13/87</td>
<td>P, F</td>
<td>50.4 Gy</td>
<td>56</td>
<td>0</td>
<td>18</td>
<td>NR</td>
<td>23</td>
</tr>
<tr>
<td>Fukuoka, Japan¹¹</td>
<td>27</td>
<td>100</td>
<td>19/81</td>
<td>P, U</td>
<td>40 Gy</td>
<td>81</td>
<td>4</td>
<td>NR</td>
<td>56</td>
<td>37 to 76</td>
</tr>
<tr>
<td>SAKK 16/01, Switzerland⁵</td>
<td>46</td>
<td>100</td>
<td>28/78</td>
<td>P, D</td>
<td>44 Gy⁺</td>
<td>59</td>
<td>5.7</td>
<td>29</td>
<td>16 to NA</td>
<td>40  24 to 55</td>
</tr>
<tr>
<td>Friedel, Germany¹</td>
<td>120</td>
<td>73</td>
<td>29/53</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subgroup stage III B</td>
<td>88</td>
<td>100</td>
<td>C, T</td>
<td>45 Gy bid + C, T</td>
<td>48</td>
<td>12</td>
<td>18</td>
<td>14 to 22</td>
<td>16  11 to 21  21</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: P, cisplatin; E, etoposide (VP-16); C, carboplatin; Vin, vindesine; NR, not reported; T, paclitaxel; bid, two times per day; SWOG, Southwest Oncology Group; IGR, Institut Gustave Roussy; F, 5-fluorouracil; Vbl, vinblastine; U, UFT (tegafur); SAKK, Swiss Group for Clinical Cancer Research; D, docetaxel; NA, not available.

*Intention to treat, percentage of enrolled patients.
⁺Accelerated radiotherapy
⁺⁺Estimated from survival curve.
• **Trimodality trials**
  - Albain Lancet 2009 (Intergroup 0139/RTOG 9309)
    - n= 202 Patients w stage T1-3pN2M0 NSCLC
    - Concurrent induction chemo (2 cycles cisplatin 50mg/m2 d1,8,29,36 and Etoposide 50mg/m2 d1-5 and 29-33) plus RT (45Gy); if no progression, pts in group 1 underwent resection and group 2 continued RT uninterrupted up to 61Gy. 2 additional cycles of cisplatin/etoposide given in both groups.
    - Primary endpoint OS
    - PFS: 12.8 vs 10.5 mo, HR 0.77, p=0.017.
    - 5 year PFS 22 vs 11% (no p value)
    - OS 23.6 mo vs 22.2 mo (HR 0.87, p=0.24).
    - 5 yr OS 27% vs 20% (OR 0.63, p=0.10)
    - With N0 status at thoracomtomy, mOS 34.4 mo, 5 yr OS 41%.
    - Death rate 2 vs 1.8%
    - Exploratory analysis, OS improved for pts undergoing lobectomy, but not pneumonectomy, vs chemo+RT
Case 3

• Trimodality trials
  - Van Meerbeeck J Natl Cancer Inst 2007 (EORTC 08941)
    - Pts w stage IIIA-N2 NSCLC were given 3 cycles of platinum based induction chemo (3 cycles of cisplatin 80mg/m2 per cycles, or carboplatin, AUC at least 5 per cycle), combined with at least one other chemotherapy drug
    - Responding pts were subsequently randomly assigned to surgical resection or RT
    - 154 pts allocated to resection and 154 to RT
    - Primary endpoint OS
    - PFS 9 vs 11.3mo (p=0.6)
    - OS 16.4 (Surgery) vs 17.5 mo (RT) 5 year OS 15.7 vs 14% HR 1.06, (p=0.6)
    - Among irradiated pts, overall compliance to RT was 55% Operative mortality of pneumonectomy 7%
    - Only 50% patients randomized to surgical resection achieved a complete resection
Case 3

• My take on this:
  - Definitive N2 disease = safe to start from chemoradiation therapy
  - Stage III with N1 disease = consult with surgeon first
  - Always discuss each case with surgeon, send to him/her after PET
  - Avoid pneumonectomy, but in select cases lobectomy can help (?)
  - No good evidence for induction chemotherapy
Case 3

• Choice of chemotherapy in chemoRT
  - No evidence for superiority
  - In BC: cisplatin/etoposide or carboplatin/paclitaxel used
  - Other regimens used in other regions (usually to lower toxicities such as esophagitis)
  - “Consolidative chemotherapy” in the PPO (controversial and not always appropriate?)
    ➢ SWOG S9504, HOG LUN – docetaxel
    ➢ SWOG 0023 – gefitinib
    ➢ CALGB 30407 – pemetrexed
    ➢ KCSG-LU05-04 (JCO 2015) – cisplatin/docetaxel
    ➢ Yamamoto ASCO 2012 (meta-analysis) – 45 phase II/III studies, negative
    ➢ (Does not this mean that there is level I evidence that fails to show evidence for consolidative chemotherapy? However, no phase III to study SAME chemo regimen used as consolidative chemotherapy so still discussed in some settings)
“In between” cases

• Fit patient with 2 ipsilateral 1cm lesions, different lobes, no lymph node involvement, after surgical resection
• Non-surgical candidate patient with 6cm lung lesion, no lymph node involvement
• Patient with multiple recurrent AIS (formerly known as BAC)
• Locoregional recurrence after surgery or SBRT
• Superior sulcus tumour
• Endobronchial or tracheal-wall limited disease
Fit patient with 2 ipsilateral 1cm lesions

Included in ANITA
Not included in BR.10
Many experts recommend no adjuvant chemotherapy if both nodules <4cm and n0
Non-surgical candidate patient with 6cm lung lesion, no lymph node involvement

Many experts recommend no chemotherapy with radiation therapy in the case of N0 or 1
Patient with multiple recurrent AIS (formerly known as BAC)

- Multiple resection vs. observation
- ?RT (currently no role if pure AIS, but what if there is solid component?)
- Difficult to biopsy safely
- Very good prognosis as long as they do not transform into invasive adenocarcinoma
Locoregional recurrence after surgery or SBRT

• Most often, still attempt to treat with curative intent if possible
Endobronchial or tracheal-wall limited disease

• Multiple ablative techniques
  - Intra-tracheal/bronchial brachytherapy
  - External beam radiation
  - Endobronchial thermal, laser or cryotherapy
Stage IV NSCLC

• Why treat? Is it worth it?
• How do we diagnose?
• How do we treat?
• What about targeted therapy?
• What about immunotherapy?
Outcomes across a decade

**TABLE 1.** Baseline Characteristics of Patients Who Received Best Supportive Care (BSC) Versus Chemotherapy by Year of Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>C1 1998</th>
<th></th>
<th>C2 2001</th>
<th></th>
<th>C3 2006</th>
<th></th>
<th>C4 2007</th>
<th></th>
<th>p across years BSC</th>
<th>p across years chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BSC</strong></td>
<td></td>
<td><strong>Chemo</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>Chemo</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n = 464</strong></td>
<td></td>
<td><strong>n = 91</strong></td>
<td></td>
<td></td>
<td><strong>n = 485</strong></td>
<td></td>
<td><strong>n = 146</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>n = 501</strong></td>
<td></td>
<td><strong>n = 249</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Median age (range)</strong></td>
<td>68 (38–93)</td>
<td>70 (39–96)</td>
<td>72 (37–95)</td>
<td>71 (43–101)</td>
<td>70 (39–96)</td>
<td>60 (35–83)</td>
<td>63 (33–86)</td>
<td>63 (34–86)</td>
<td>&lt;0.005</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td><strong>Gender (female/male)</strong></td>
<td>199/265</td>
<td>198/287</td>
<td>200/253</td>
<td>213/288</td>
<td>125/110</td>
<td>123/126</td>
<td>0.78</td>
<td>0.38</td>
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</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Squamous</td>
<td>102 (22%)</td>
<td>115 (24%)</td>
<td>84 (19%)</td>
<td>71 (14%)</td>
<td>20 (14%)</td>
<td>41 (17%)</td>
<td>0.48</td>
<td>0.22</td>
<td></td>
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</tr>
<tr>
<td>Non-squamous</td>
<td>229 (49%)</td>
<td>200 (41%)</td>
<td>156 (34%)</td>
<td>139 (28%)</td>
<td>91 (62%)</td>
<td>108 (46%)</td>
<td>94 (38%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>133 (29%)</td>
<td>170 (35%)</td>
<td>213 (47%)</td>
<td>291 (58%)</td>
<td>20 (22%)</td>
<td>35 (24%)</td>
<td>133 (53%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>43 (10%)</td>
<td>253 (53%)</td>
<td>182 (40%)</td>
<td>215 (43%)</td>
<td>9 (10%)</td>
<td>64 (44%)</td>
<td>88 (35%)</td>
<td>0.006</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>30 (6%)</td>
<td>170 (35%)</td>
<td>205 (45%)</td>
<td>214 (43%)</td>
<td>15 (16%)</td>
<td>61 (42%)</td>
<td>107 (45%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>6 (1%)</td>
<td>34 (7%)</td>
<td>43 (9%)</td>
<td>44 (9%)</td>
<td>7 (8%)</td>
<td>17 (11%)</td>
<td>50 (20%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Unknown</td>
<td>385 (83%)</td>
<td>28 (6%)</td>
<td>23 (6%)</td>
<td>28 (5%)</td>
<td>60 (66%)</td>
<td>4 (3%)</td>
<td>3 (2%)</td>
<td>2 (1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Eastern Cooperative Group Performance Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>83 (18%)</td>
<td>129 (27%)</td>
<td>136 (30%)</td>
<td>120 (24%)</td>
<td>34 (37%)</td>
<td>88 (60%)</td>
<td>148 (59%)</td>
<td>0.003</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>144 (31%)</td>
<td>355 (73%)</td>
<td>315 (69%)</td>
<td>381 (76%)</td>
<td>23 (25%)</td>
<td>55 (38%)</td>
<td>92 (39%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>237 (51%)</td>
<td>1 (3%)</td>
<td>2 (1%)</td>
<td>9 (4%)</td>
<td>34 (38%)</td>
<td>3 (2%)</td>
<td>4 (2%)</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>28 (6%)</td>
<td>33 (7%)</td>
<td>48 (11%)</td>
<td>42 (8%)</td>
<td>7 (8%)</td>
<td>7 (5%)</td>
<td>44 (18%)</td>
<td>0.053</td>
<td>&lt;0.005</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>436 (94%)</td>
<td>452 (93%)</td>
<td>405 (89%)</td>
<td>459 (92%)</td>
<td>84 (92%)</td>
<td>139 (95%)</td>
<td>205 (82%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ho J Thorac Oncol. 2014;9: 1180–1186
Outcomes across a decade

<table>
<thead>
<tr>
<th>Table 2. Description of Types of Chemotherapy Administered in First, Second and Third Line by Year of Diagnosis (p Value Across Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
</tr>
<tr>
<td>First line n (%)</td>
</tr>
<tr>
<td>Median number of cycles</td>
</tr>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Platinum/etoposide</td>
</tr>
<tr>
<td>Platinum/taxane</td>
</tr>
<tr>
<td>Platinum/vinorelbine</td>
</tr>
<tr>
<td>Platinum/gemcitabine</td>
</tr>
<tr>
<td>Epidermal growth factor receptor TKI</td>
</tr>
<tr>
<td>Single agent/other</td>
</tr>
<tr>
<td>Second line n (%)</td>
</tr>
<tr>
<td>Median number of cycles</td>
</tr>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Platinum doublet</td>
</tr>
<tr>
<td>Docetaxel</td>
</tr>
<tr>
<td>Epidermal growth factor receptor TKI</td>
</tr>
<tr>
<td>Pemetrexed</td>
</tr>
<tr>
<td>Single agent/other</td>
</tr>
<tr>
<td>Third line n (%)</td>
</tr>
<tr>
<td>Median number of cycles</td>
</tr>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Platinum doublet</td>
</tr>
<tr>
<td>Docetaxel</td>
</tr>
<tr>
<td>Epidermal growth factor receptor TKI</td>
</tr>
<tr>
<td>Pemetrexed</td>
</tr>
<tr>
<td>Single agent/other</td>
</tr>
</tbody>
</table>

TKI, tyrosine kinase inhibitor.
Outcomes across a decade
Outcomes across a decade

B

Overall survival by year: Chemotherapy

<table>
<thead>
<tr>
<th>Year</th>
<th>Median OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>9.4 m</td>
</tr>
<tr>
<td>2001</td>
<td>9.8 m</td>
</tr>
<tr>
<td>2006</td>
<td>11.0 m</td>
</tr>
<tr>
<td>2007</td>
<td>11.8 m</td>
</tr>
</tbody>
</table>

$p=0.023$
Perception with stage IV lung cancer

• n=672 physicians

TABLE 1. Participating Physician Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Physicians Answering Breast Cancer Questionnaire (n = 352)</th>
<th>Physicians Answering Lung Cancer Questionnaire (n = 320)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years of practice</td>
<td>644</td>
<td>15.82</td>
<td>14.93</td>
</tr>
<tr>
<td>Number of patients per week</td>
<td>665</td>
<td>77.30</td>
<td>80.00</td>
</tr>
<tr>
<td>Number of breast cancer patients per year</td>
<td>653</td>
<td>7.61</td>
<td>7.12</td>
</tr>
<tr>
<td>Number of lung cancer patients per year</td>
<td>652</td>
<td>4.12</td>
<td>3.58</td>
</tr>
<tr>
<td>Gender</td>
<td>664</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>634</td>
<td>37</td>
<td>35</td>
</tr>
<tr>
<td>Male (%)</td>
<td></td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>Age (yr)</td>
<td></td>
<td>634</td>
<td>46.30</td>
</tr>
</tbody>
</table>

Perception with stage IV lung cancer

<table>
<thead>
<tr>
<th></th>
<th>Physicians Answering Breast Cancer Questionnaire</th>
<th>Physicians Answering Lung Cancer Questionnaire</th>
<th>Physicians Answering Nonsmoking Questionnaire</th>
<th>Physicians Answering Smoking Questionnaire</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of cancer</td>
<td>655</td>
<td>2.47</td>
<td>2.59</td>
<td>0.185</td>
<td>655</td>
</tr>
<tr>
<td>Degree of symptoms</td>
<td>654</td>
<td>2.99</td>
<td>3.16</td>
<td>0.115</td>
<td>649</td>
</tr>
<tr>
<td>Patient’s desire for referral</td>
<td>652</td>
<td>2.18</td>
<td>2.27</td>
<td>0.496</td>
<td>652</td>
</tr>
<tr>
<td>Patient’s age</td>
<td>652</td>
<td>3.24</td>
<td>3.37</td>
<td>0.258</td>
<td>652</td>
</tr>
<tr>
<td>Patient’s comorbid medical conditions</td>
<td>650</td>
<td>2.95</td>
<td>3.05</td>
<td>0.380</td>
<td>650</td>
</tr>
<tr>
<td>Distance patient has to travel for the referral</td>
<td>646</td>
<td>3.51</td>
<td>3.64</td>
<td>0.235</td>
<td>646</td>
</tr>
</tbody>
</table>

The following scale was used for quantification of the physicians’ decision: 1 = extremely important in my decision making about referral; 2 = very important; 3 = somewhat important; 4 = not too important; 5 = not at all important in my decision making about referral.
Perception with stage IV lung cancer

**FIGURE 1.** Number of patients with advanced-stage breast or lung cancer and with both good (<2) and poor (>2) performance status who would be referred to a medical oncologist.
Perception with stage IV lung cancer

**FIGURE 2.** Percentage of physicians who felt that the patients with both early-stage and metastatic disease would have improved survival with chemotherapy.
More effective treatment

• Palliative care
• Palliative care
• Palliative care

• Chemotherapy
• Targeted therapy
  - Two genetic mutations currently in use to find targeted therapy: EGFR/ALK
• Immunotherapy
• Palliative RT
More effective treatment

• Chemotherapy
  - 4 cycles of platinum doublet +/- maintenance chemotherapy
  - Contemporary OS: 14 months

2013 JCO Paz-Ares LG
More effective treatment

• EGFR mutation
  - Generally non-smoker, younger, Asian female patients but still present in smoker, older, non-Asian male patients (~10-15%)
  - Need to test everyone
  - Asian patients – need to be very persistent in obtaining the testing (>20%, and in non-smoker females, up to 50%)
More effective treatment

• EGFR mutation
  - Contemporary OS 19 months, PFS 9 months
  - Potentially even longer with third-generation EGFR TKI (PFS 19m!)

More effective treatment

• ALK mutation
  - 3%
  - However, if positive, ALK inhibitor very effective (similar numbers as EGFR TKIs)

2014 ASCO/NEJM Mok/Solomon
Laboratory Services

Laboratory Services provides diagnostic laboratory and cervical cancer screening laboratory services.

About  Test request forms  Accreditation
These forms are updated regularly, they can also be found under the appropriate section heading. Please only use the current form and do not write in other tests that are not on the form. All files are in pdf format.

**Cancer genetics**

- [Cancer Genetics Hematological Request Form](#)

- [Cancer Genetics Solid Tumour Request Form](#)
  
  The following are now on the above form please do not use old forms: ALK/EGFR; BRAF; GIST; KRAS

- [Cancer Genetics RET index testing requisition](#)
### SOLID TUMOUR TESTING REQUISITION

See [www.cancergeneticslab.ca](http://www.cancergeneticslab.ca) for current Myeloid, Lymphoid, Solid Tumor and Hereditary test information and requisitions.

**Requesting Physician:** Please complete and sign this requisition and then fax to the originating hospital lab holding the specimen.

**Lab:** Please ship specimen with copies of this form and path report to: BCCA Pathology - Room 3225, 600 West 10th Avenue, Vancouver BC V5Z 4E6

### PATIENT INFORMATION

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First and Middle Names</th>
<th>Name</th>
<th>MSC</th>
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<tbody>
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</table>

<table>
<thead>
<tr>
<th>Date of Birth dd/mmm/yyyy</th>
<th>Sex</th>
<th>PHN</th>
<th>BCCA ID#</th>
<th>Phone</th>
<th>Fax</th>
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</table>

### SPECIMEN

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Originating Hospital</th>
<th>Referring lab/Hospital Sample ID</th>
<th>Collection Date dd/mmm/yyyy</th>
<th>Tissue Type</th>
<th>Tumour Content</th>
<th>Tumour Cellularity</th>
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<tbody>
<tr>
<td>FFFE/Block</td>
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<tr>
<td>CGL Specimen</td>
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<tr>
<td>Other ________</td>
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</tr>
</tbody>
</table>

### COPY PHYSICIANS (ALL INFORMATION IS NECESSARY)

<table>
<thead>
<tr>
<th>Name</th>
<th>MSC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

### REASON FOR TESTING/DIAGNOSIS/CLINICAL HISTORY (REQUIRED FOR TEST TO PROCEED)

### MOLECULAR

Select Oncopanel OR single-gene testing, both cannot be performed. Samples with limiting DNA may instead receive single-gene testing for the provided indication.

Tests requiring less than 14 day turnaround should select single-gene assay.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Oncopanel (14-21 days)</th>
<th>Single-gene testing (&lt;14 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal Cancer (Metastatic)</td>
<td>Oncopanel</td>
<td>KRAS (codons 12,13)</td>
</tr>
<tr>
<td>Gastrointestinal Stromal Tumour (GIST)</td>
<td>Oncopanel</td>
<td>KIT</td>
</tr>
<tr>
<td>Glioblastoma Multiforme</td>
<td>Oncopanel</td>
<td>MGMT promoter methylation</td>
</tr>
<tr>
<td><strong>Low Grade Glioma</strong></td>
<td>Oncopanel</td>
<td></td>
</tr>
<tr>
<td><strong>Lung Cancer (Stage IIIB/IV Non-Squamous, Non-Neuroendocrine)</strong></td>
<td>Oncopanel, PDL1, ALK IHC/2p23 FISH</td>
<td>EGF, PDL1, ALK IHC/2p23 FISH</td>
</tr>
<tr>
<td><strong>Melanoma (Non-Resectable/Metastatic)</strong></td>
<td>Oncopanel</td>
<td>BRAF (V600 E,D,K)</td>
</tr>
</tbody>
</table>

### CYTOGENETICS (FISH)

- Tumor DNA FISH
- Copy-Number Fluorescence In Situ Hybridization
- Oncogene Activation
- Tumor and Host DNA FISH
- Single-Gene FISH
Immunotherapy
Attempts (successes)

• Cancer vaccine (Sipuleucel T)
• Adaptive cell transfer (CAR cell therapy)
• Therapeutic antibodies (trastuzumab emtansine)
• Immune system modulator (IFN alpha, IL-2)
And now..

• Checkpoint inhibitors

• = stop the immune system breaks or regulatory/suppressor signals
Despite Advances, Only Small Incremental OS Benefits in Overall Patient Population

- **First-line combination with chemotherapy**
- **After failure of one prior chemotherapy**
- **Maintenance treatment after first-line chemotherapy**
- **First-line or unspecified setting single agent**

**Timeline**

- **1970**: Cisplatin*
- **1978**: Carboplatin*
- **1980**: Vinorelbine 1994
- **1989**: Docetaxel 1999
- **1990**: Paclitaxel 1998
- **1992**: Gemcitabine 1996
- **1994**: Docetaxel 2002
- **1999**: Erlotinib 2004
- **2000**: Gefitinib†
- **2002**: Pemetrexed‡
- **2003**: Carboplatin*
- **2004**: Docetaxel 2010
- **2005**: Bevacizumab‡
- **2006**: Pemetrexed‡
- **2007**: Nab-Paclitaxel 2012
- **2009**: Pemetrexed‡
- **2010**: Afatinib***
- **2011**: Crizotinib†
- **2012**: Eribulin**
- **2013**: Afatinib***
- **2014**: Pemetrexed‡
- **2015**: Lutetium-177 DOTATATE

**Median OS, months**

- **1970**: ~2–4
- **1980**: ~6
- **1990**: ~8–10
- **2000**: 12+
- **2010**: 13+

**Note:**

*Not approved in NSCLC, but commonly used; †Restricted to patients participating in a clinical trial or continuing to benefit from treatment already initiated; ‡Non-squamous NSCLC only; §ALK-positive NSCLC only; **EGFR exon 19 deletions or exon 21 (L858R) substitution mutations only; #Afatinib is approved for the treatment of patients with activating EGFR mutations but only PFS data have been published (May 2014).

T-cell Checkpoint Regulation

- T-cell responses are regulated through a complex balance of inhibitory ("checkpoint") and activating signals.
- Tumours can dysregulate these pathways and consequently, the immune response.
- Targeting these pathways is an evolving approach to cancer therapy.

Immune Escape in Cancer

Many tumours escape the immune response by creating an immunosuppressive microenvironment that prevents an effective antitumour response\textsuperscript{1,2}

Recruitment of immunosuppressive cells
- Tregs
- MDSCs

Ineffective presentation of tumour antigens to the immune system
- Downregulation of MHC Expression
- Suppression of APC

Release of immunosuppressive factors
- Factors/enzymes directly or indirectly suppress immune response

Tumour Cells

Tumour Microenvironment

The mechanisms tumours use to escape the immune system provide a range of potential therapeutic targets for cancer

APC=antigen-presenting cell; MDSC=myeloid-derived suppressor cell; MHC=major histocompatibility complex; Treg=regulatory T cell.

Checkpoint inhibitors

Immune cells

Regulatory signals

Cancer

Immune cells

Cancer
Checkpoint inhibitors

• T regulatory signals

Priming phase = CTLA4

Tumour microenvironment checkpoint = Programmed Death pathway
Immuno-oncology: Blocking CTLA-4 and PD-1 Pathways with Monoclonal Antibodies

CTLA-4 pathway blockade

PD-1 pathway blockade

CTLA-4=cytotoxic T-lymphocyte antigen-4; PD-1=programmed cell death 1; PD-L1/2=PD ligand 1/2; TCR=T cell receptor.
CTLA-4 inhibitor = ipilimumab etc

Antigen presentation and ligation of B7/CD28 co-activators results in T-cell activation

In the activated T cell, CTLA-4 competes with CD28 and acts as the brakes on T-cell activation by binding to B7

By inhibiting CTLA-4, ipilimumab releases the natural braking system and restores T-cell activation, allowing T-cell proliferation to continue

B7: B7.1 (CD80) or B7.2 (CD86)

CTLA-4 = cytotoxic T-lymphocyte-associated antigen-4; MHC = major histocompatibility complex; TCR = T-cell receptor.

PD-1 and PD-L1 Antibodies = nivolumab, pembrolizumab, atezolizumab etc

- PD-1 – inhibitory receptor found on activated lymphocytes and monocytes and is associated with tumour immune escape
- Binds with PD-L1 on tumour cells
- Interaction between PD-1 and PD-L1 suppresses the cytotoxic T-cell response

Adapted from *N Engl Med*. 2012;366(26):2517
Overall Survival with Nivolumab vs. Docetaxel for Pretreated Non-squamous NSCLC Patients: Phase III Randomized Study

- Nivolumab decreased risk of death by 27% in pretreated, non-squamous NSCLC vs. docetaxel.
- Nivolumab significantly improved overall survival of patients with non-squamous NSCLC by 2.8 months vs. docetaxel.

Symbols represent censored observations. 
Overall Survival with Nivolumab vs. Docetaxel for Pretreated Squamous NSCLC Patients: Phase III, Randomized Study

- Nivolumab decreased risk of death by 41% vs. docetaxel at 1 year and 38% at 18 months
- Nivolumab significantly improved median overall survival by 3.2 months vs. docetaxel.

Reckamp K et al. Presented at World Lung Conference. 2015; Based on August 2015 DBL; symbols refer to censored observations.
Pembrolizumab vs. chemotherapy in first-line NSCLC PD-L1 \( \geq 50\% \)

6m survival 80.2 vs 72.4%

**Figure 2.** Overall Survival in the Intention-to-Treat Population.
Shown are Kaplan–Meier estimates of overall survival, according to treatment group. Tick marks represent data censored at the last time the patient was known to be alive. The intention-to-treat population included all patients who underwent randomization.

OS (≥5% PD-L1+)
CheckMate 026: Nivolumab vs Chemotherapy in First-line NSCLC

- 60.4% in the chemotherapy arm had subsequent nivolumab therapy
- 43.6% in the nivolumab arm had subsequent systemic therapy

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab n = 211</th>
<th>Chemotherapy n = 212</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS, months</td>
<td>14.4 (11.7, 17.4)</td>
<td>13.2 (10.7, 17.1)</td>
</tr>
<tr>
<td>1-year OS rate, %</td>
<td>56.3</td>
<td>53.6</td>
</tr>
</tbody>
</table>

HR = 1.02 (95% CI: 0.80, 1.30)

All randomized patients (≥1% PD-L1+): HR = 1.07 (95% CI: 0.86, 1.33)

Socinski ESMO 2016
Better and earlier palliative care

- We need more palliative care
- On ALL stage IV lung cancer consultations, we need to do the following upfront:
  - Address advance care planning
  - Connect them with palliative home care
  - Apply for palliative benefit
  - Patient needs ongoing and continual face to face support from their primary care physicians (unfortunately, due to time spent in cancer centre, disconnect happens often)
  - Pain and symptom management clinic at BCCA
Better and earlier palliative care

- Patient lives LONGER due to earlier palliative care
- Reduces distress and anxiety by patient and caregiver
- Reduces inappropriate ICU, CPR, critical care
- Patient better prepares for end of life care
- Increased patient satisfaction
- Better and faster response to patient symptom (it is NOT good enough to be able to see cancer patients with significant symptoms in 2-3 weeks)
- Total suffering, spiritual and psychological care

2010 Temel NEJM, 2014 Zimmerman Lancet Oncol
Better and earlier palliative care

The ‘surprise’ question in advanced cancer patients: A prospective study among general practitioners

Matteo Moroni1,2
Donato Zocchi3
Deborah Bolognesi4
Amy Abernethy5
Roberto Rondelli6
Giandomenico Savorani3
Marcello Salera3
Filippo G Dall'Olio7
Giulia Galli7
Guido Biasco2,7
on behalf of the SUQ-P group3

Moroni Palliat Med July 2014 vol. 28 no. 7 959-964
Better and earlier palliative care

**Table 2.** Sensitivity, specificity, predictive value of the ‘surprise’ question (231 evaluable cases).

<table>
<thead>
<tr>
<th>Group</th>
<th>Living</th>
<th>Deceased</th>
<th>Predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Yes’</td>
<td>88</td>
<td>17</td>
<td>Positive 83.8% CI: 75.3–90.3</td>
</tr>
<tr>
<td>‘No’</td>
<td>39</td>
<td>87</td>
<td>Negative 69.0% CI: 60.2–77.0</td>
</tr>
</tbody>
</table>

CI: confidence interval.
Sensitivity = 69.3% (CI: 60.5–77.2); specificity = 83.6% (CI: 75.1–90.2); Matthews correlation coefficient (MCC) = 0.53.

Log-rank P < 0.0001

Mean (±SE) Days Alive

- “Yes” = 346.9 ± 5.9
- “No” = 214.8 ± 14.2
Better and earlier palliative care

Table 4. Multivariate Cox regression to predict status at 1 year.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of cancer (pancreas)</td>
<td>2.228</td>
<td>0.772–6.432</td>
<td>0.139</td>
</tr>
<tr>
<td>Surprise question (reference = yes)</td>
<td>6.978</td>
<td>2.418–20.134</td>
<td>0.000</td>
</tr>
</tbody>
</table>

CI: confidence interval.
Summary

• Vigilance for potential high risk patients in cancer screening and early diagnosis
• Streamlined FAST diagnostic workup
• Effective treatments on the horizon... but only 1/3 get to them
• EARLY and effective primary and palliative care is critical.
Thank you!