Adjuvant Chemotherapy and Adjuvant Radiation Therapy for Stages I-IIIA Resectable Non-Small Cell Lung Cancer Guideline

Cancer Care Ontario and American Society of Clinical Oncology
Introduction

• The Cancer Care Ontario (CCO) Program in Evidence-based Care (PEBC) and the American Society of Clinical Oncology (ASCO) convened an expert panel in August 2006 to review the evidence and draft recommendations on the role of adjuvant chemotherapy and adjuvant radiation therapy for completely resected stages I-IIIA non-small cell lung cancer (NSCLC).

• CCO originally published guidelines in 1997 and updated them in 2004-2006.

• Both CCO-PEBC and ASCO conducted external reviews of the current guidelines.
Guideline Methodology: Systematic Review

• An ASCO Update Committee completed a review and analysis of data published since 2000 to August 2006:

  ✓ Evidence-based practice guidelines
  ✓ Randomized Controlled trials
  ✓ Meta-Analyses
### Guideline Methodology: Panel Members

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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*The guideline manuscript is dedicated to Dr. Christopher E. Desch.*
2007 Recommendations for Adjuvant Treatment of Stages I-IIIA NSCLC

Clinical Questions

1. What is the benefit in terms of overall survival of adjuvant chemotherapy in patients with completely resected stages I – IIIA non-small cell lung cancer?

2. What is the benefit in terms of overall survival of adjuvant radiation therapy in patients with completely resected stages I – IIIA non-small cell lung cancer?

3. What roles should adjuvant chemotherapy and adjuvant radiation therapy play in completely resected stages I – IIIA non-small cell lung cancer?
2007 Recommendations for Adjuvant Treatment of Stages I-III A NSCLC

Adjuvant Cisplatin-Based Chemotherapy

- **Stage IA**: Adjuvant chemotherapy is not recommended.
- **Stage IB**: Adjuvant cisplatin-based chemotherapy is not recommended for routine use.
- **Stage IIA**: Adjuvant cisplatin-based chemotherapy is recommended.
- **Stage IIB**: Adjuvant cisplatin-based chemotherapy is recommended.
- **Stage III A**: Adjuvant cisplatin-based chemotherapy is recommended.
- The use of adjuvant chemotherapy regimens that include alkylating agents is not recommended as these agents have been found to be detrimental to survival.

- Recommendations apply only to completely resected tumors.
Recommended Dose: Adjuvant Chemotherapy for Stages IIA-IIIA NSCLC

Cisplatin-Vinorelbine

- Cisplatin: 50 mg/m² on days 1 and 8 every four weeks for four cycles, and
- Vinorelbine: 25 mg/m² weekly for 16 weeks for four cycles
- Considerations:
  - Convenience for patients
  - Patients’ resource constraints
  - The use of one cisplatin-based chemotherapy regimen consistently in order to ensure familiarity and optimize patient safety
2007 Recommendations for Adjuvant Treatment of Stages I-IIIA NSCLC: Adjuvant Radiotherapy

- **Stages IA/B and IIA/B**: Adjuvant radiation is not recommended.

- **Stage IIIA**: Adjuvant radiation therapy is not recommended for routine use because of the lack of prospective, randomized clinical trial data evaluating its efficacy. A clinical trial is underway to determine the advisability of its routine use.

  - Recommendations apply only to completely resected tumors.
2007 Recommendations for Adjuvant Treatment of Stages I-IIIA NSCLC

Special Considerations

• Patients with poor performance status
• Patients with advanced age
Strategies to Improve Doctor-Patient Communication

- Therapeutic nihilism towards adjuvant chemotherapy for stages II-III NSCLC should now be abandoned
- Recognize that unique issues face people with lung cancer
- Offer a session devoted solely to discussing patient’s prognosis and the risks and benefits of adjuvant chemotherapy

**This section is consensus-based, rather than evidence-based**
Strategies to Improve Doctor-Patient Communication

• Patients with cancer generally prefer shared-decision making
• Present patients with individualized descriptions of their risks and benefits
• Graphs included in guideline to help physicians communicate the absolute risk and benefit of adjuvant chemotherapy for the various stages of NSCLC

**This section is consensus-based, rather than evidence-based**
Strategies to Improve Doctor-Patient Communication, cont’d

• With the physician providing immediate guidance and interpretation, a graph may help patients achieve a better understanding of absolute risk and benefit.

• Graphical Representations*

• Source: LACE meta-analysis

• Using LACE data to estimate absolute benefit, adjuvant chemotherapy raises 5-year survival from 64% to 67% for stage IB NSCLC, from 39% to 49% for stage II NSCLC, and from 26% to 39% for stage III NSCLC
Strategies to Improve Doctor-Patient Communication, cont’d

- Graphs separate patient sample into groups:
  - Those who die within 5 years whether they receive chemotherapy or not (white)
  - Those who live without receiving chemotherapy (yellow)
  - Those who live because of chemotherapy (green)

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
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<tbody>
<tr>
<td>33</td>
<td>51</td>
<td>61</td>
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Notes: The figures are a graphical representation of patient survival probabilities at 5 years: the combined yellow and green areas represents the survival probability for the treatment group \(S_a\) (the yellow represents the survival probability for untreated patients \(S_c\), green represents the absolute risk reduction \(S_a - S_c\), i.e., the “extra” survival achieved by therapy), the white area represent the mortality probability in patients \(1 - S_a\). The statistical uncertainty in these probabilities is not depicted in the figures. Calculations for these figures included data on untreated patients from the ANITA trial because these data were not available in the LACE abstract. *Includes the three trials that included only stage IB, does not include two trials open for stages IA and IB.
Selective Review of Molecular Markers in NSCLC

• Panel undertook selective review of the literature pertaining to seven molecular markers

• The majority were investigated for their possible ability to predict cisplatin resistance

• Currently there is a lack of conclusive evidence showing that any marker is significantly related to clinical outcome
## Summary

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<tr>
<th>Stage</th>
<th>Not Recommended</th>
<th>Recommended</th>
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| IA    | • Adjuvant chemotherapy  
|       | • Adjuvant radiation therapy  
|       | • Alkylating agents                                                           |                                                  |
| IB    | • Adjuvant cisplatin-based chemotherapy on a routine basis  
|       | • Adjuvant carboplatin-based chemotherapy  
|       | • Adjuvant radiation therapy  
|       | • Alkylating agents                                                           |                                                  |
| IIA   | • Adjuvant carboplatin-based chemotherapy  
|       | • Adjuvant radiation therapy  
|       | • Alkylating agents                                                           | • Adjuvant cisplatin-based chemotherapy          |
| IIB   | • Adjuvant carboplatin-based chemotherapy  
|       | • Adjuvant radiation therapy  
|       | • Alkylating agents                                                           | • Adjuvant cisplatin-based chemotherapy          |
| IIIA  | • Adjuvant carboplatin-based chemotherapy  
|       | • Adjuvant radiation therapy for routine use  
|       | • Alkylating agents                                                           | • Adjuvant cisplatin-based chemotherapy          |
Additional ASCO Resources

- The full text of the guideline, this slide set, a Decision Aid Tool*, and additional resources are available at: http://www.asco.org/guidelines/adjuvantnsclc

- A Patient Guide on Adjuvant Treatment for Lung Cancer can be found at http://www.cancer.net

- *A version of Adjuvant! has been produced to make estimates of NSCLC patient outcomes with and without adjuvant therapy (1,2,3). We have for the publication of these guidelines produced our own version of such a tool.


  2) A computer program designed to assist in NSCLC adjuvant therapy decision making. P. M. Ravdin Abstract - No. 7230. 2006 ASCO Annual Meeting

  3) http://www.adjuvantonline.com
It is important to realize that many management questions have not been comprehensively addressed in randomized trials and guidelines cannot always account for individual variation among patients. A guideline is not intended to supplant physician judgment with respect to particular patients or special clinical situations and cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at obtaining the same results. Accordingly, ASCO considers adherence to this guideline to be voluntary, with the ultimate determination regarding its application to be made by the physician in light of each patient’s individual circumstances. In addition, the guideline describes administration of therapies in clinical practice; it cannot be assumed to apply to interventions performed in the context of clinical trials, given that clinical studies are designed to test innovative and novel therapies in a disease and setting for which better therapy is needed. Because guideline development involves a review and synthesis of the latest literature, a practice guideline also serves to identify important questions for further research and those settings in which investigational therapy should be considered.