

Cancer Care Ontario Practice Guidelines Initiative

Sponsored By: Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care



Unresected Stage III Non-Small Cell Lung Cancer

Practice Guideline Report #7-3

ORIGINAL GUIDELINE: March 14, 1997

MOST RECENT LITERATURE SEARCH: December 2002

NEW EVIDENCE ADDED TO GUIDELINE REPORT: January 2003

RECOMMENDATIONS LAST MODIFIED: The recommendations have not been modified since the original guideline was developed.

The Lung Disease Site Group is rewriting this practice guideline report and may revise the recommendations. The rewritten guideline report will include new evidence on the use of palliative radiotherapy, hyperfractionated radiotherapy, and accelerated radiotherapy in the treatment of unresected stage III disease, as well as evidence on the sequencing of chemotherapy relative to radiotherapy in combined modality regimens. **When completed, the new practice guideline report will replace the current report.**

SUMMARY

Guideline Questions

1. What is the role of different schedules or doses of radiotherapy in patients with unresected, clinical or pathological stage III NSCLC? (Note: unresected stage III NSCLC is defined as: tumours that, for either technical or medical reasons, cannot be completely resected; either clinical or pathological stage III NSCLC.)
2. Does chemotherapy combined with radiation therapy improve survival compared with radiation therapy alone in patients with unresected NSCLC?

Target Population

These recommendations apply to adult patients with unresected clinical or pathological stage III non-small cell lung cancer. (Note: unresected stage III NSCLC is defined as: tumours that, for either technical or medical reasons, cannot be completely resected; either clinical or pathological stage III NSCLC.)

Recommendations

Key Recommendation

- Patients with good performance status (ECOG 0 to 1) and minimal weight loss (less than 5% in the preceding three months) have been shown to have a survival benefit from treatment with combined chemo-radiotherapy and should be considered for this type of treatment approach. For these selected patients, thoracic irradiation of 60 Gy in 30 fractions over a six-week period in combination with cisplatin-based chemotherapy is recommended as a

treatment option. A full discussion should occur between the patient and physician concerning the benefits, limitations, and toxicities of therapy.

Qualifying Statements

- Patients not fitting the above criteria are not candidates for combined modality treatment. Those experiencing symptoms amenable to treatment should receive palliative thoracic irradiation.
- At this time, hyperfractionated radiation is not recommended outside the context of a clinical trial.

Methods

Entries to MEDLINE (through December 2002), CANCERLIT (through October 2002) and Cochrane Library (2002, Issue 4) databases have been searched for evidence relevant to this practice guideline. The most recent literature search was performed in January 2003.

Evidence was selected and reviewed by four members of the Cancer Care Ontario Practice Guidelines Initiative's (CCOPGI) Lung Cancer Disease Site Group (Lung DSG) and methodologists. This practice guideline has been reviewed and approved by the Lung DSG, which comprised medical and radiation oncologists, pathologists, surgeons, epidemiologists, a medical sociologist, and a psychologist at the time the guideline was developed. At that time, patients were not represented. Community representatives participated in the updating of the practice guideline report.

External Review by Ontario practitioners was obtained through a mailed survey. Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee (PGCC).

The CCOPGI has a formal standardized process to ensure the currency of each guideline report. This process consists of periodic review and evaluation of the scientific literature and, where appropriate, integration of this literature with the original guideline information.

Key Evidence

- One meta-analysis detected a statistically significant overall benefit at two years for the use of combined chemo- and radiotherapy compared with radiotherapy alone. A hazard ratio of 0.90 (95% confidence interval, 0.83 to 0.97) or a 10% reduction in the risk of death translated into an absolute benefit of 3% at two years and 2% at five years. Subgroup analysis comparing combined chemo- and radiotherapy with cisplatin-containing regimens versus radiotherapy alone demonstrated a 13% reduction in the risk of death in the combined treatment arm (pooled hazard ratio, 0.87; 95% confidence interval, 0.79 to 0.96). This represents an absolute benefit of 4% at 2 years.
- Toxicity from chemotherapy and/or radiotherapy is largely confined to neutropenic-related infection, weight loss, and vomiting. Serious infections requiring hospitalization and weight loss are more prevalent in combined modality therapy (sequential chemo-radiotherapy) compared to radiation alone. Patients receiving concurrent combined chemo-radiotherapy may also be at risk for radiation pneumonitis and esophagitis.
- A second meta-analysis detected a statistically significant advantage to cisplatin-based combination chemotherapy compared with chemotherapy alone. In the cisplatin-based combination chemotherapy group, the reduction in mortality at one and two years was 24% and 30%, with an odds ratio for death of 0.76 (95% confidence interval, 0.6 to 0.9) at one year and 0.70 (95% confidence interval, 0.5 to 0.9) at two years. A third meta-analysis showed a statistically significant advantage to combined modality therapy over radiotherapy alone. The overall relative risk of death for combined modality therapy was 0.87 (95%

confidence interval, 0.81 to 0.94; 13% reduction in relative risk) at two years and 0.83 (95% confidence interval, 0.77 to 0.90; 17% reduction in relative risk) at three years, in favour of combined chemo-radiotherapy.

Related Guidelines

Cancer Care Ontario Practice Guidelines Initiative Practice Guideline Report #7-12: *Altered Fractionation of Radical Radiation Therapy in the Management of Unresectable Non-Small Cell Lung Cancer*.

Prepared by the Lung Cancer Disease Site Group

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PREAMBLE: About Our Practice Guideline Reports

The Cancer Care Ontario Practice Guidelines Initiative (CCOPGI) is a project supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care, as part of the Program in Evidence-based Care. The purpose of the Program is to improve outcomes for cancer patients, to assist practitioners to apply the best available research evidence to clinical decisions, and to promote responsible use of health care resources. The core activity of the Program is the development of practice guidelines by multidisciplinary Disease Site Groups of the CCOPGI using the methodology of the Practice Guidelines Development Cycle.¹ The resulting practice guideline reports are convenient and up-to-date sources of the best available evidence on clinical topics, developed through systematic reviews, evidence synthesis and input from a broad community of practitioners. They are intended to promote evidence-based practice.

This practice guideline report has been formally approved by the Practice Guidelines Coordinating Committee, whose membership includes oncologists, other health providers, community representatives and Cancer Care Ontario executives. Formal approval of a practice guideline by the Coordinating Committee does not necessarily mean that the practice guideline has been adopted as a practice policy of CCO. The decision to adopt a practice guideline as a practice policy rests with each regional cancer network that is expected to consult with relevant stakeholders, including CCO.

Reference:

1. Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. *J Clin Oncol* 1995;13(2):502-12.

For the most current versions of the guideline reports and information about the CCOPGI and the Program, please visit our Internet site at:

<http://www.cancercare.on.ca/ccopgi/>

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