Complete Summary

GUIDELINE TITLE

The role of photodynamic therapy (PDT) in patients with non-small cell lung cancer: a clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

Maziak DE, Markman BR, Mackay JA, Evans WK, Lung Cancer Disease Site Group. The role of photodynamic therapy (PDT) in patients with non-small cell lung cancer: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2005 Nov 1. Various p. (Evidence-based series; no. 7-15). [27 references]

GUIDELINE STATUS

This is the current release of the guideline.

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Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Primary, non-small cell lung cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology
Radiation Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To evaluate the role for photodynamic therapy (PDT) in the management of early stage lung cancer
- To evaluate the role for PDT in the palliation of patients with symptomatic, locally advanced lung cancer

TARGET POPULATION

Adult patients with primary, non-small cell lung tumours

INTERVENTIONS AND PRACTICES CONSIDERED

1. Photodynamic therapy
2. Monitor for adverse effects

MAJOR OUTCOMES CONSIDERED

- Response rate
- Survival
- Toxicity
- Palliation of symptoms for locally advanced lung cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search Strategy

MEDLINE (1966 through June 2005), CANCERLIT (1975 through June 2002), EMBASE (1988 through 2005, week 23) and the Cochrane Library (2005, Issue 4)

databases were searched. "Lung neoplasms" (Medical subject heading (MeSH)) was combined with "bronchial neoplasms" (MeSH), "dihematoporphyrin ether" (MeSH), "hematoporphyrins" (MeSH), "hematoporphyrin photoradiation" (MeSH), "phototherapy" (MeSH) and each of the following phrases used as text words: "lung cancer," "lung carcinoma," "lung malignancy," "bronchogenic cancer," "bronchial cancer," "bronchogenic carcinoma," "bronchial carcinoma," "bronchogenic malignancy," "bronchial malignancy," "photofrin," "porphrin," "porphyrin," "hematoporphyrin," "dihematoporphyrin ether," "porfimer sodium." These terms were then combined with the search terms for the following study designs: practice guidelines, systematic or quantitative reviews, meta-analyses, randomized controlled trials, controlled clinical trials, clinical trials phase ii and phase iii, and multicenter studies.

In addition, conference proceedings of the American Society of Clinical Oncology (ASCO) were searched for abstracts of relevant trials published between 1997 through 2005. The Physician Data Query (PDQ) clinical trials database on the Internet (http://www.cancer.gov/search/clinical_trials/) was searched for reports of new or ongoing trials. The Canadian Medical Association Infobase (http://mdm.ca/cpgsnew/cpgs/index.asp) and the National Guideline Clearinghouse (http://www.guideline.gov) were searched for existing evidence-based practice guidelines.

Relevant articles and abstracts were selected and reviewed by two reviewers, and the reference lists from those sources were searched for additional trials, as were the reference lists from relevant review articles.

Inclusion Criteria

Fully published reports or abstracts that met the following criteria were selected for inclusion:

1. Systematic reviews, practice guidelines, randomized controlled trials (RCTs) or noncontrolled prospective studies of photodynamic therapy (PDT) using porfimer sodium (Photofrin®), alone or in combination with other therapies, for the treatment of stages I through IV primary, non-small cell lung cancers
2. Outcomes of survival, response rate, or toxicity were reported, or for locally advanced lung cancer, the outcome of symptom palliation was reported

Exclusion Criteria

1. Studies with less than ten patients
2. Studies in which photodynamic therapy was used for the detection of lung cancer
3. Individual case reports, pilot studies and retrospective studies
4. Letters and editorials
5. Papers published in a language other than English

NUMBER OF SOURCE DOCUMENTS

Two evidence-based guidelines, three randomized controlled trials (RCTs) in patients with late stage lung cancer, eleven non-controlled studies reporting for

early stage lung cancer (three reported in a single abstract), one summary paper reporting the cumulative results of photodynamic therapy (PDT) studies in early stage disease conducted in Japan over 19 years, one non-controlled study that included a mix of stages, and four non-controlled studies of PDT in late stage disease met the inclusion criteria.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The three randomized trials identified in the literature search did not have similar treatment comparisons; therefore, a meta-analysis of this data was not considered appropriate. In addition, the other prospective trials identified in the literature search were non-comparative and were not suitable for meta-analysis.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Program in Evidence-based Care (PEBC) reports consist of a comprehensive systematic review of the clinical evidence on a specific cancer care topic, an interpretation of and consensus agreement on that evidence by Disease Site Groups and Guideline Development Groups, the resulting clinical recommendations and an external review by Ontario clinicians in the province for whom the topic is relevant.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

An earlier version of the practice guideline and systematic review, dated February 26, 2002 was circulated to Ontario clinicians for feedback. Feedback was obtained through a mailed survey of 114 practitioners in Ontario (37 medical oncologists, 22 radiation oncologists, 29 surgeons, 25 respirologists, and one hematologist). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. The survey was mailed out on February 26, 2002. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Lung Disease Site Group (DSG) reviewed the results of the survey.

The evidence summary report was circulated to members of the Practice Guidelines Coordinating Committee (PGCC) for review and approval. All 11 members of the PGCC returned ballots. Six PGCC members approved the evidence summary report as written, three members approved the report as written and provided suggestions for consideration by the Lung DSG, and two members approved the report conditional on the Lung DSG addressing specific concerns. The Lung DSG responded to the PGCC concerns as detailed in the original guideline document and the evidence summary was subsequently approved.

The final recommendations were developed by the Lung DSG and approved by the DSG and the PGCC.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The lack of sufficient high-quality evidence precludes definitive recommendations. Instead, the Lung Cancer Disease Site Group (DSG) offers the following opinions based on the evidence reviewed:

- Photodynamic therapy could be considered as an option for the treatment of early-stage lung cancer in patients with medically inoperable disease that is accessible by bronchoscopy. Evidence to date suggests that photodynamic therapy may be most effective with small superficial airway lesions, 1cm or less in length. The relative safety and effectiveness of photodynamic therapy compared to radiotherapy, an alternative treatment for patients with inoperable early stage disease, remains undefined.
- In locally advanced and symptomatic lung cancer, photodynamic therapy can contribute to the relief of airway obstruction and hemoptysis, but its role is, as yet, not well defined in relation to other modalities of palliation.
- Serious adverse effects including fatal hemoptysis and respiratory failure can occur; therefore, the suitability of patients for this treatment should be carefully assessed. Since tumour necrosis can result in post-treatment airway

obstruction, patients should be closely monitored after undergoing the procedure and toilet bronchoscopies repeated as indicated.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by evidence-based guidelines, randomized controlled trials (RCTs), non-controlled studies, and one summary paper.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Eleven non-controlled studies and one summary paper reporting on the use of photodynamic therapy in early stage lung cancer patients, who generally could not tolerate surgery or refused surgery, showed that photodynamic therapy commonly leads to tumour regression. The reported five-year survival rates in these patients varied from 43.4% to 72%.
- In patients with late stage lung cancer, three randomized controlled trials and four noncontrolled studies showed that photodynamic therapy could contribute to the palliation of local cancer-related symptoms. Of the three randomized trials, two comparing photodynamic therapy with neodymium-yttrium aluminum garnet (Nd:YAG) laser therapy and one comparing photodynamic therapy plus external beam radiotherapy with external beam radiotherapy alone, none detected a survival advantage for photodynamic therapy; however, photodynamic therapy did produce improved pulmonary symptom control. There was a significant improvement in the control of hemoptysis and the relief of dyspnea for patients receiving photodynamic therapy plus radiotherapy compared with those receiving radiotherapy alone.

POTENTIAL HARMS

The most common adverse effect reported in all studies was photosensitivity, which consisted mostly of sunburn. The most serious adverse effects reported were respiratory failure and hemoptysis. The former, resulting from airway edema and tumour necrosis, led to mechanical ventilation in three of 67 patients with early stage lung cancer (two studies). Fatal hemoptysis occurred within one month of treatment in seven of 213 patients (two studies), three with early stage disease and four with locally advanced lung cancer. Three of 20 patients with locally advanced lung cancer also suffered from fatal hemoptysis between two and 18 months post-treatment. The role of photodynamic therapy in producing late fatal hemoptysis is uncertain.

CONTRAINDICATIONS

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Contraindications for photodynamic therapy include porphyria or known allergies to porphyrins, tumours that impact on major blood vessels, and existing tracheoesophageal fistulas.

QUALIFYING STATEMENTS

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Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the evidence-based series is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding their content or use or application and disclaims any for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Nov 1

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Lung Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The primary authors of this guideline report declared no potential conflicts of interest.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- The role of photodynamic therapy (PDT) in patients with non-small cell lung cancer. Evidence-based series report. Toronto (ON): Cancer Care Ontario (CCO), 2005 Nov 1. Various p. (Practice guideline; no. 7-15: Section 1). Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- 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.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 24, 2006. The information was verified by the guideline developer on February 23, 2006.

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