Complete Summary

GUIDELINE TITLE

Small cell lung cancer.

BIBLIOGRAPHIC SOURCE(S)

Simon GR, Wagner H. Small cell lung cancer. Chest 2003 Jan;123(1 Suppl):259S-71S. [103 references]

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SCOPE

DISEASE/CONDITION(S)

Small cell lung cancer

GUIDELINE CATEGORY

Diagnosis
Treatment

CLINICAL SPECIALTY

Oncology
Pulmonary Medicine
Radiation Oncology
Thoracic Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide clinically relevant, evidence-based guidelines for the staging and treatment of small cell lung cancer (SCLC)

TARGET POPULATION

Patients with or suspected of having small cell lung cancer (SCLC)

INTERVENTIONS AND PRACTICES CONSIDERED

Routine Staging Procedures

1. Medical history and physical examination
2. Complete blood counts
3. Comprehensive chemistry panels
4. Computed tomography (CT) scan (chest and abdomen)
5. Computed tomography scan or magnetic resonance imaging (MRI) of the brain
6. Bone scan

Treatment

Extensive-stage Small Cell Lung Cancer (SCLC)

1. First-line platinum-based chemotherapy (e.g., cisplatin-etoposide-carboplatin, paclitaxel-etoposide, platinum, cisplatin-irinotecan, cisplatin-vinblastine-mitomycin-C, cisplatin-etoposide-all-trans-retinoic acid, cisplatin-docetaxel, cisplatin-paclitaxel, topotecan)
2. Prophylactic cranial irradiation (PCI) for patients with a complete remission
3. Further chemotherapy for relapsed or refractory SCLC (e.g., etoposide-irinotecan, cisplatin-topotecan, etoposide-hexamethylmelamine, irinotecan-paclitaxel, carboplatin-paclitaxel, cyclophosphamide-adriamycin-vincristine)

Limited-stage SCLC

1. Referral to a radiation oncologist and medical oncologist for chemotherapy and radiation therapy
2. Prophylactic cranial irradiation for patients with a complete remission
3. Surgical resection for very limited-stage disease following mediastinoscopy

Therapies Considered but Not Recommended

1. The use of granulocyte colony-stimulating factor (G-CSF)
2. Non-platinum-based chemotherapy regimens as first-line treatment in extensive disease

Therapies Considered but Not Recommended Outside of a Clinical Trial

1. Dose-dense/intense initial/induction or maintenance treatment for patients with extensive- or limited-stage SCLC
2. The use of positron emission tomography (PET) scanning for routine staging

MAJOR OUTCOMES CONSIDERED

- Accuracy and utility of staging procedures for small cell lung cancer
- Survival
- Response rates (complete and partial response rates)
- Relapse rates

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

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

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

As a first step in identifying the evidence for each topic, the guideline developers sought existing evidence syntheses including guidelines, systematic reviews, and meta-analyses. They searched computerized bibliographic databases including MEDLINE, Cancerlit, CINAHL and HealthStar, the Cochrane Collaboration Database of Abstracts of Reviews of Effectiveness, the National Guideline Clearinghouse, and the National Cancer Institute Physician Data Query database. Computerized searches through July 2001 used the MeSH terms lung neoplasms (exploded) and bronchial neoplasms or text searches for lung cancer combined with review articles, practice guidelines, guidelines, and meta-analyses. They also searched and included studies from the reference lists of review articles, and queried experts in the field. An international search was conducted of Web sites of provider organizations that were likely to have developed guidelines. Abstracts of candidate English language articles were reviewed by two physicians (one with methodological expertise and one with content area expertise) and a subset was selected for review in full text. Full-text articles were reviewed again by two physicians to determine whether they were original publications of a synthesis and were pertinent to at least one of the topics of the guideline. Articles described as practice guidelines, systematic reviews, or meta-analyses were included, as were review articles that included a "Methods" section. Included articles were classified according to topic.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The United States Preventive Services Task Force (USPSTF) scheme offers general guidelines to assign one of the following grades of evidence: good, fair, or poor.

In general, good evidence included prospective, controlled, randomized clinical trials, and poor evidence included case series and clinical experience. Trials with fair quality of evidence, for instance, historically controlled trials or retrospective analyses, were somewhere in between. In addition to the strength of the study design, however, study quality also was considered. The United States Preventive Services Task Force approach considers well-recognized criteria in rating the quality of individual studies for a variety of different types of study design (e.g., diagnostic accuracy studies and case-control studies). The thresholds for distinguishing good vs fair and fair vs poor evidence are not explicit but are left to the judgment of panelists, reviewers, and members of the executive committee.

Assessment of the Scope and Quality of Clinical Practice Guidelines

Clinical practice guidelines identified from the systematic search were evaluated by at least four reviewers using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Each writing committee received a comprehensive list of existing systematic reviews and meta-analyses as well as guidelines published by other groups. In addition, for five key topics (prevention, screening, diagnosis, and staging [invasive and noninvasive]), new systematic reviews were undertaken (see "Description of Methods Used to Collect the Evidence" and "Description of Methods Used to Analyze the Evidence" fields). For all other topics, writing committees were responsible for identifying and interpreting studies that were not otherwise covered in existing syntheses or guidelines.

The guidelines developed by the writing committee were distributed to the entire expert panel, and comments were solicited in advance of a meeting. During the meeting, proposed recommendations were reviewed, discussed, and voted on by the entire panel. Approval required consensus, which was defined as an overwhelming majority approval. Differences of opinion were accommodated by revising the proposed recommendation, the rationale, or the grade until consensus could be reached. The evidence supporting each recommendation was summarized, and recommendations were graded as described. The assessments of level of evidence, net benefit, and grade of recommendation were reviewed by the executive committee.

Values

The panel considered data on functional status, quality and length of life, tolerability of treatment, and relief of symptoms in formulating guideline recommendations. Cost was not explicitly considered in the guideline development process. Data on these outcomes were informally weighted, without the use of explicit decision analysis or other modeling. The values placed on types of outcomes varied with clinical scenarios. For example, in some situations they considered life expectancy, such as the effects of early detection. In other situations they weighed quality of life more heavily, such as in palliative care and in interpreting small increases in life expectancy with chemotherapy for stage IV disease.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The guideline developer´s grading scheme is a modification of the United States Preventive Services Task Force (USPSTF) grades to allow recommendations for a service when (1) evidence is poor, (2) the assessment of the net benefit is moderate to high, and (3) there is consensus among the expert panel to recommend it. This change was necessary because, unlike preventive services (i.e., the routine offering of tests or treatments to well people) in which the burden of proof is high, clinical decisions about the treatment of patients with lung cancer often must be based on an interpretation of the available evidence, even if it is of poor quality. This adaptation distinguished between interventions with poor evidence for which there is consensus (grade C) and interventions with poor evidence for which there is not consensus (grade I).

Grades of Recommendations and Estimates of Net Benefit

The grade of the strength of recommendations is based on both the quality of the evidence and the net benefit of the service (i.e., test, procedure, etc).

Grade A The panel strongly recommends that clinicians routinely provide [the service] to eligible patients. An "A" recommendation indicates good evidence that [the service] improves important health outcomes and that benefits substantially outweigh harms.

Grade B The panel recommends that clinicians routinely provide [the service] to eligible patients. A "B" recommendation indicates at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

Grade C The panel recommends that clinicians routinely provide [the service] to eligible patients. A "C" recommendation indicates that there was consensus among the panel to recommend [the service] but that the evidence that [the service] is effective is lacking, of poor quality, or conflicting, or the balance of benefits and harms cannot be reliably determined from available evidence.

Grade D The panel recommends against clinicians routinely providing [the service]. A "D" recommendation indicates at least fair evidence that [the service] is ineffective or that harm outweighs benefit.

Grade I The panel concludes that the evidence is insufficient to recommend for or against [the service]. An "I" recommendation indicates that evidence that [the service] is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined, and that the panel lacked a consensus to recommend it.

Net Benefit

The levels of net benefit are based on clinical assessment. Estimated net benefit may be downgraded based on uncertainty in estimates of benefits and harms.

Substantial Benefit: Benefit greatly outweighs harm

Moderate Benefit: Benefit outweighs harm

Small/weak Benefit: Benefit outweighs harm to a minimally clinically important degree

None/negative Benefit: Harms equal or outweigh benefit, less than clinically important

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After extensive review within the expert panel and executive committee, the guidelines were reviewed and approved by the American College of Chest Physicians (ACCP) Health and Science Policy Committee and then by the American College of Chest Physicians Board of Regents.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is rated based on the levels of evidence (good, fair, poor), net benefit (substantial, moderate, small/weak, none/negative), and the grades of the recommendations (A, B, C, D, I). Definitions are presented at the end of the "Major Recommendations" field.

Staging of Small SCLC

1. In all patients, routine staging of small cell lung cancer (SCLC) should include history and physical examinations, complete blood counts, a comprehensive

chemistry panel, a computed tomography (CT) scan of the chest and abdomen, a CT or magnetic resonance imaging (MRI) scan of the brain, and a bone scan. Level of evidence, good; benefit, substantial; grade of recommendation, A
2. For the routine staging of patients with SCLC, positron emission tomography (PET) scanning is not recommended outside of a clinical trial. Level of evidence, fair; benefit, none/negative; grade of recommendation, D

Treatment of Extensive-Stage SCLC

First-Line Treatment

3. Patients with extensive-stage disease should receive platinum-based chemotherapy. Level of evidence, good; benefit, substantial; grade of recommendation, A
4. Patients achieving a complete remission (CR) should be offered prophylactic cranial irradiation (PCI). Level of evidence, fair; benefit, small; grade of recommendation, C

Maintenance Treatment

5. For patients with extensive-stage or limited-stage SCLC achieving a partial response or a CR, there is no evidence, outside of a clinical trial, for the use of maintenance treatment. Level of evidence, good; benefit, none/negative; grade of recommendation, D

Treatment of Relapsed or Refractory SCLC

6. Patients with SCLC who have relapsed following an initial response to treatment or who are refractory to the initial treatment should be offered further chemotherapy. The chemotherapy offered will depend on the duration of the response after receiving first-line chemotherapy or the lack of response to first-line chemotherapy (i.e., sensitive relapses vs refractory patients). Level of evidence, fair; benefit, small/weak; grade of recommendation, C

Treatment of Elderly (> 70 years of age) Patients With Extensive-Stage SCLC

7. Elderly patients with good performance status and with intact organ function should be treated with platinum-based chemotherapy. Level of evidence, good; benefit, moderate; grade of recommendation, B
8. Elderly patients with poor prognostic factors such as poor performance status or severe concomitant comorbid disease may still be considered for chemotherapy. Level of evidence, poor; benefit, small; grade of recommendation, C
9. Elderly patients achieving a CR should be offered PCI. Level of evidence, fair; benefit, small; grade of recommendation, C

Dose Intensity in SCLC

10. For patients with either extensive-stage or limited-stage SCLC, there is no role for the administration of dose-dense/intense, initial/induction, or maintenance treatment outside of a clinical trial. Level of evidence, good; benefit, none/ negative; grade of recommendation, D

The Role of Growth Factor and the Use of Stem Cell Support in SCLC

11. In patients with SCLC who are receiving chemotherapy, the routine use of growth factor is not recommended. Level of evidence, good; benefit, none/negative; grade of recommendation, D

Treatment of Limited-Stage SCLC

12. Patients with limited-stage SCLC should be referred to a radiation oncologist and a medical oncologist for chemotherapy and radiation therapy. Level of evidence, good; benefit, substantial; grade of recommendation, A
13. Patients with limited-stage SCLC achieving a CR should be offered PCI. Level of evidence, good; benefit, substantial; grade of recommendation, A

Prophylactic Cranial Irradiation

14. Patients with limited-stage SCLC achieving a CR or patients who have undergone resection who have stage I disease should be offered PCI. Level of evidence, good; benefit, substantial; grade of recommendation, A
15. Patients with extensive-stage SCLC achieving a CR should be offered PCI. Level of evidence, fair; benefit, small; grade of recommendation, C

Role of Surgery in Early-Stage SCLC

16. For the rare patient with very limited-stage disease (i.e., T1-2,N0 tumors), surgical resection followed by platinum-based chemotherapy could be offered. Level of evidence, fair; benefit, small; grade of recommendation, C
17. Mediastinoscopy should be performed in all patients undergoing surgical resection. Level of evidence, poor; benefit, moderate; grade of recommendation, C
18. PCI should be offered to patients achieving a CR. Level of evidence, fair; benefit, small; grade of recommendation, C

Definitions:

Levels of Evidence

In general, good evidence included prospective, controlled, randomized clinical trials, and poor evidence included case series and clinical experience. Trials with fair quality of evidence, for instance, historically controlled trials or retrospective analyses, were somewhere in between.

Grades of Recommendations and Estimates of Net Benefit

The grade of the strength of recommendations is based on both the quality of the evidence and the net benefit of the service (i.e., test, procedure, etc).

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Grade C The panel recommends that clinicians routinely provide [the service] to eligible patients. A "C" recommendation indicates that there was consensus among the panel to recommend [the service] but that the evidence that [the service] is effective is lacking, of poor quality, or conflicting, or the balance of benefits and harms cannot be reliably determined from available evidence.

Grade D The panel recommends against clinicians routinely providing [the service]. A "D" recommendation indicates at least fair evidence that [the service] is ineffective or that harm outweighs benefit.

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None/negative Benefit: Harms equal or outweigh benefit, less than clinically important

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Limited-stage small cell lung cancer can be optimally treated with a concurrent chemotherapy and radiation therapy approach, and approximately 20% of patients can be cured.
- The use of prophylactic cranial irradiation (PCI) has been shown to provide a small absolute benefit in survival in patients who achieve complete remission.

POTENTIAL HARMS

Toxicity of Chemotherapy

- Carboplatin plus etoposide is as effective as cisplatin plus etoposide but is less toxic (except for increased myelosuppression).
- The addition of ifosfamide to cisplatin and etoposide in a phase III trial of 171 patients with extensive stage disease caused increased toxicity but also increased 2-year survival from 5 to 13%.
- A study comparing the use of paclitaxel, etoposide, and platinum with the use of etoposide and platinum alone was terminated early because of a higher number of toxic deaths in the triple-therapy arm of the study. Another study showed an increased incidence of toxic deaths when paclitaxel was added to cisplatin and etoposide.
- Elderly patients experience greater myelosuppression than do younger counterparts at equivalent drug exposures.

Toxicity of Radiation Therapy

The dose-limiting toxicity of radiation therapy is acute esophagitis.

Prophylactic Cranial Irradiation (PCI)

Earlier trials of PCI had variably reported late neurotoxicity, with deterioration in memory, calculation ability, and quality of life. The relation of these toxicities to treatment was unclear. In several more recent trials in which cognitive function was assessed prospectively, significant differences between small cell lung cancer patients and age-matched and gender-matched control subjects have been observed prior to any treatment, with up to 40% of patients showing significant impairment. Significant further deterioration following PCI was not seen in a large 1997 trial in the United Kingdom. Van Oosterhout et al performed careful neurologic and neurophysiologic examinations of 59 survivors who were alive >2 years after receiving a diagnosis and who underwent a cranial computed tomography or magnetic resonance imaging scan. Groups were neurophysiologically compared with matched control subjects. The authors concluded that although more intensively systemically treated patients showed more neurologic impairment, there was no statistical evidence for additional neurotoxicity with PCI.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

1. The American College of Chest Physicians (ACCP) is developing a set of PowerPoint slide presentations for physicians to download and use for physician and allied health practitioners education programs.
2. The ACCP is developing a Quick Reference Guide (QRG) in print and PDA formats for easy reference.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Simon GR, Wagner H. Small cell lung cancer. Chest 2003 Jan;123(1 Suppl):259S-71S. [103 references]

ADAPTATION

Not applicable: Guideline was not adapted from another source.

DATE RELEASED

2003 Jan

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

GUIDELINE DEVELOPER COMMENT

The guideline development panel was composed of members and nonmembers of the American College of Chest Physicians (ACCP) who were known to have expertise in various areas of lung cancer management and care, representing multiple specialties from the following 13 national and international medical associations:

- Alliance for Lung Cancer Advocacy, Support, and Education (a patient support group)
- American Association for Bronchology
- American Cancer Society
- American College of Physicians
- American College of Surgeons Oncology Group
- American Society of Clinical Oncology
- American Society for Therapeutic Radiology and Oncology
- American Thoracic Society
- Association of Community Cancer Centers
- Canadian Thoracic Society
- National Comprehensive Cancer Network
- Oncology Nurses Society
- Society of Thoracic Surgeons

The specialties included pulmonary/respiratory medicine, critical care, medical oncology, thoracic surgery, radiation oncology, epidemiology, law, and medical ethics.

SOURCE(S) OF FUNDING

Funding for both the evidence reviews and guideline development was provided through an unrestricted educational grant from Bristol-Myers Squibb, which had no other role in the evidence review or guideline development process or content.

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: George R. Simon, MD, FCCP; Henry Wagner, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Information about potential conflicts of interest were collected from each member of the expert panel or writing committee at the time of their nomination in accordance with the policy of the American College of Chest Physicians (ACCP). Information on conflicts of interest for each panelist is listed in the guideline.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Background Articles

- Alberts WM. Lung cancer guidelines. Introduction. Chest 2003 Jan;123(1 Suppl):1S-2S
- McCrory DC, Colice GL, Lewis SZ, Alberts WM, Parker S. Overview of methodology for lung cancer evidence review and guideline development. Chest 2003 Jan;123(1 Suppl):3S-6S.
- Harpole LH, Kelley MJ, Schreiber G, Toloza EM, Kolimaga J, McCrory DC. Assessment of the scope and quality of clinical practice guidelines in lung cancer. Chest 2003 Jan;123(1 Suppl):7S-20S.
- Alberg AJ, Samet JM. Epidemiology of lung cancer. Chest 2003 Jan;123(1 Suppl):21S-49S.

Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 3, 2003. The information was verified by the guideline developer on October 1, 2003.

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