Chemotherapy for Relapsed Small Cell Lung Cancer

Members of the Lung Cancer Disease Site Group

An assessment conducted in December 2016 deferred the review of Evidence-based Series (EBS) 7-17 Version 2, which means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document.

(PEBC Assessment & Review Protocol)

This document is available on the CCO web site (http://www.cancercare.on.ca) and is comprised of the following 4 sections:

Section 1: Clinical Practice Guideline (ENDORSED)
Section 2: Systematic Review
Section 3: Guideline Development and External Review
Section 4: Document Review Summary and Tool

Release Date: May 16, 2013

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## Guideline Report History

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Chemotherapy for Relapsed Small Cell Lung Cancer: Guideline Recommendations

S. Cheng, W.K. Evans, D. Stys-Norman, F.A. Shepherd, and the Lung Cancer Disease Site Group

A Quality Initiative of the Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)
Developed by the Lung Cancer Disease Site Group

These guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Summary and Review Tool for a summary of updated evidence published between 2005 and 2012, and for details on how this Clinical Practice Guideline was ENDORSED.

Report Date: December 11, 2012

Questions
1. In patients with relapsed small cell lung cancer (SCLC), does chemotherapy improve survival and quality of life?
2. Which single-agent or combination chemotherapy regimen is most effective in the treatment of relapsed SCLC?
3. Which patients with relapsed SCLC are most likely to benefit from additional chemotherapy?

Target Population
These recommendations apply to adult patients with relapsed SCLC.

Recommendations
• The evidence for the clinical benefit of second-line chemotherapy in the treatment of patients with relapsed SCLC is limited. The selection of patients for treatment with second-line therapy should be dependent on the treatment-free interval, the extent of
response to first-line therapy, residual toxicity from first-line therapy, and the performance status of the patient.

- There is insufficient evidence to recommend a specific chemotherapy regimen. However, in the opinion of the Lung Cancer Disease Site Group, patients who relapse three or more months following the completion of first-line chemotherapy may benefit from retreatment with the same regimen that induced their initial response. This would generally mean retreatment with etoposide-cisplatin. Alternative regimens may include cyclophosphamide, doxorubicin, and vincristine (CAV) or carboplatin and etoposide.

- Oral topotecan is a possible alternative for patients who initially responded to chemotherapy and had a response duration of 45 days or longer.

- There is insufficient evidence to determine whether one mode of administration of topotecan is superior to any other mode of administration. Oral administration is more convenient and may be a treatment option for patients not suitable for intravenous therapy. Oral administration is associated with a higher incidence of grade 3/4 diarrhea, whereas intravenous administration may result in a higher frequency of grade 3/4 neutropenia.

- There is currently no standard second-line chemotherapy regimen for patients who fail to respond to or who relapse shortly after first-line therapy. Clinical trials are needed to determine the optimal treatment regimen.

**Key Evidence**

- One randomized phase III trial compared chemotherapy to best supportive care, three randomized trials (one phase II and two phase III) compared different second-line chemotherapy regimens, and two randomized trials (one phase II and one phase III) compared different forms of administration of second-line single-agent chemotherapy.

- One recent randomized phase II trial showed that chemotherapy consisting of oral topotecan and best supportive care (BSC) extended survival when compared with BSC alone [26 versus 14 weeks, hazard ratio (HR), 0.64; 95% confidence interval (CI), 0.45-0.90; p=0.0104] and improved the quality of life for patients who had relapsed, resistant SCLC. The response rate for patients treated with oral topotecan and BSC was only 7%.

- One randomized phase II trial comparing cisplatin and etoposide to carboplatin, cisplatin, and etoposide found no significant differences in response rate (p=0.20) or survival (p=0.11).

- One randomized phase III trial that treated patients with CAV or topotecan alone reported no significant differences in response rate (p=0.285) or survival (p=0.795).

- One phase III trial randomized patients to either bis-chloro-ethyl-nitrosourea [BCNU], thiotepa, vincristine, cyclophosphamide (BTOC) or etoposide and cisplatin; no significant differences in response rate (p=0.91) or survival (p=0.15) were found.

- Two randomized trials (phase II and phase III) compared oral to intravenous (IV) administration of topotecan. Response rates were 18.3% and 23.1% for oral administration and 14.8% and 21.9% for IV administration. Survival was not significantly different between the modes of administration (HR, 0.98; 95% CI, 0.77-1.25; and risk ratio, 0.84; 95% CI, 0.53-1.32).

**Related Guidelines**
- # 7-13-1: The Role of Combination Chemotherapy in the Initial Management of Limited-Stage Small-Cell Lung Cancer;
- # 7-13-2: Prophylactic Cranial Irradiation in Small Cell Lung Cancer;
- # 7-13-3: The Role of Thoracic Radiotherapy as an Adjunct to Standard Chemotherapy in Limited-Stage Small Cell Lung Cancer.

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