SUPERIOR SULCUS (PANCOAST) TUMOURS

Effective Date: January, 2012

The recommendations contained in this guideline are a consensus of the Alberta Provincial Thoracic Tumour Team synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

BACKGROUND

Lung cancer is the overall leading cause of cancer mortality in Canadian men and women. By the end of 2011, an estimated 25,300 new cases of lung cancer will be diagnosed in Canada.[1] In addition, an estimated 20,600 Canadian men and women will die from their disease; a total higher than the estimated deaths from prostate, breast, and colorectal cancers combined.[1] Despite many research and clinical advances in lung cancer treatments, the age-standardized five-year survival rate for all types and stages of lung cancer combined is only 16 percent for Canada overall, and 14 percent for Alberta.[1] The economic impact of lung cancer care is equally as staggering: the mean cost associated with the care of each patient diagnosed with lung cancer in Alberta is reported to be $15,350 for non-small cell lung cancer and $18,243 for small cell lung cancer, not including end-of-life care.[2] Smoking remains the largest single risk factor for lung cancer, responsible for 90 percent of lung cancers in men and 80 percent of lung cancers in women in Canada. Exposure to specific industrial and atmospheric pollutants, including second-hand tobacco smoke, also increases an individual's risk of lung cancer.

Lung cancer can be classified into non-small cell lung cancer (NSCLC) or small-cell lung cancer (SCLC). NSCLC accounts for 80 percent of all lung cancer cases, and is categorized using the TNM staging system, which was recently updated by the International Association for the Study of Lung Cancer (IASLC). The staging definitions and stage groups for NSCLC are summarized in a supporting document (NSCLC Staging System).

Superior sulcus tumours of the lung (T3-4, N0-1), often termed Pancoast tumours, occur in less than 5 percent of all non-small cell lung cancer cases.[3] These tumours arise from the apex of the lung, cause specific symptoms and signs, and are among the most challenging thoracic tumours to treat because of their involvement with adjacent vital structures. However, patients with Pancoast tumours, particularly T3, N0 disease, *are* amenable to curative treatment; overall survival rates have been reported to be between 30 and 70 percent, depending on the types of therapies used.

GUIDELINE QUESTIONS

- What are the recommended treatment options for patients with superior sulcus (Pancoast) tumours?

DEVELOPMENT AND REVISION HISTORY

This guideline was reviewed and endorsed by the Alberta Provincial Thoracic Tumour Team. Members of the Alberta Provincial Thoracic Malignancy Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Thoracic Tumour Team and a Knowledge Management Specialist from the Guideline Utilization Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook.

This guideline was originally developed in July, 2008. This guideline was revised in September, 2009 and January, 2012.

SEARCH STRATEGY

For this guideline update, a search for new or updated practice guidelines published since September 2009 was conducted by accessing the websites of the following organizations: Cancer Care Ontario (CCO), British Columbia Cancer Agency (BCCA), Cancer Care Nova Scotia (CCNS), the National Comprehensive Cancer Network (NCCN), the Scottish Intercollegiate Guidelines Network (SIGN), the National Institute for Health and Clinical Excellence (NICE), the American College of Chest Physicians (ACCP), the Australian Cancer Network, and the European Society for Medical Oncology (ESMO).

Medical journal articles were searched using Medline Ovid (2009-2012), EMBASE (2009-2012), Cochrane Database of Systematic Reviews, and PubMed electronic databases; the references and bibliographies of articles identified through these searches were scanned for additional sources. The search terms included: Pancoast, Superior Sulcus, Lung Neoplasms [MeSH heading], Carcinoma, Non-Small Cell Lung [MeSH heading], practice guidelines, systematic reviews, meta-analyses, randomized controlled trials, and clinical trials. Articles were excluded from the final review if they: had a non-English abstract, were not available through the library system, were a case study involving less than 5 patients, or were published prior to January 2009.

TARGET POPULATION

The recommendations in this guideline apply to adult patients over the age of 18 years.

RECOMMENDATIONS

1. Whenever possible, patients should be considered for eligibility in ongoing clinical trials.

Operable:

2. If medically and surgically operable, patients should undergo pre-operative chemo-radiation.
   - Radiation dose: 45 Gy/ 25 fractions
   - Chemotherapy: cisplatin-etoposide (cisplatin 50 mg/m^2 days 1, 8, 29, 36; etoposide 50 mg/m^2 days 1-5 and 29-33)
   - To be followed by surgery 3-7 weeks after the completion of chemo-radiation.
3. For patients in whom surgery is no longer an option after completing pre-operative chemo-radiation or in the case of positive margins, boost radiation is recommended.

Inoperable – Curative Intent:

4. For patients who are inoperable or who refuse surgery, chemo-radiation is recommended provided the patient can tolerate it.
   - Cisplatin-based chemotherapy (with either etoposide or vinorelbine) and thoracic radiation of 55 Gy/ 25 fractions to 66 Gy/ 33 fractions is the recommended treatment option.

Inoperable – Palliative:

5. In patients where lung reserve or effusion precludes radical radiotherapy, palliative chemotherapy and/or palliative radiotherapy are recommended.
6. Palliative chemotherapy options include:
   - First line: platinum-based doublets
   - Second line: docetaxel, erlotinib or pemetrexed

7. For symptomatic patients with poor performance status (ECOG > 2) and/or significant weight loss (usually defined as > 10% in preceding 3 months), radiotherapy for symptom palliation is recommended.
   - Commonly used dose-fractionation schedules include 20 Gy/ 5 fractions and 30 Gy/ 10 fractions. Other dose-fractionation schedules may be used at the discretion of the radiation oncologist.
   - Single fractions of radiotherapy less than 10 Gy may be appropriate in some clinical circumstances, such as poor performance status or patient travel distance.
   - In selected cases, split course radiation can be used for palliation.

DISCUSSION

Multimodality Treatment for Operable Patients

For patients with superior sulcus tumours who are suitable for surgery, the Alberta Provincial Thoracic Tumour Team recommends the combination of pre-operative chemo-radiation followed by surgical resection (recommendation #2). In a large multimodality trial of induction chemo-radiation followed by surgery (SWOG 9416), Rusch *et al.* reported high rates of complete resection (61 of 65 patients with T3 tumours; 22 of 23 patients with T4 tumours) and pathologic complete response (56%).[4] Five-year survival was 44 percent for all patients and 54% after complete resection, with no difference between T3 and T4 tumours. In addition, pathologic complete response led to better survival compared to when there was residual disease (RR=2.14, p=.02). In this study, thoracotomy was performed between three and five weeks after induction chemo-radiation. In a recent review, Rusch suggests that surgical resection is warranted by an experienced thoracic surgeon between three and seven weeks after induction therapy, a recommendation which the Alberta Provincial Thoracic Malignancy Tumour Team has also adopted.[3]

In a second trial of multimodality treatment (JCOG 9806), 75 patients were treated with induction therapy (mitomycin C, vindesine, cisplatin) combined with radiotherapy at a dose of 45 Gy.[5] Of the 57 patients who underwent surgical resection, complete resection was achieved in 51, and 12 patients achieved pathologic complete response. Three- and five-year overall survival rates in this study were 61 and 56 percent, respectively.[5]

The results of these two large trials, findings from a restrospective case study conducted by Li et al. (2010)[12], along with similar results from single-institution studies,[6-9] have led to a new standard of care with promising results for patients with operable superior sulcus tumours. Kappers et al. (2011) also conclude in their retrospective study that multimodal therapy inclusive of radiation, chemotherapy and surgery on patients with operable Pancoast tumours offers the best treatment outcome.[13]

Chemo-radiation for Inoperable Patients

In patients with inoperable superior sulcus tumours, or those who refuse surgery, definitive chemo-radiation is recommended. The schedule of chemo-radiation recommended by the Alberta Provincial Thoracic Tumour Team follows that which is outlined for stage III NSCLC. As stated in recommendation #4, for patients with good performance status (ECOG 0-2), minimal weight loss, good pulmonary reserve, and tumour and anatomy conformation permitting radical dose radiation without expected severe normal tissue toxicity, cisplatin-based chemotherapy (with either etoposide or vinorelbine) and thoracic radiation in the range of 55 Gy/ 25 fractions to 66 Gy/ 33 fractions is the recommended treatment option.

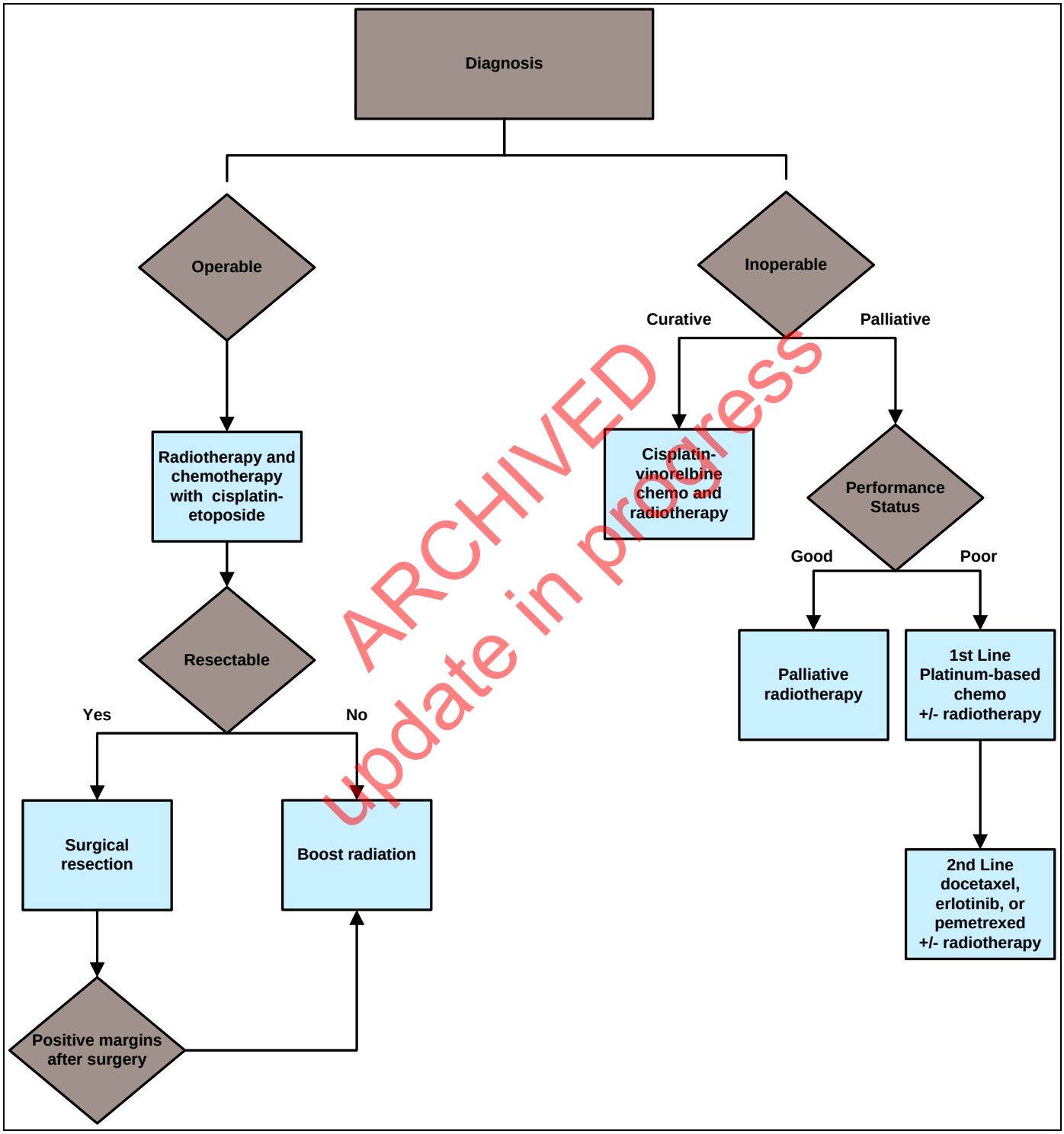
In patients where surgery is no longer an option after completing preoperative chemo-radiation, or where there are positive margins, a boost to the radiation dose is recommended (recommendation #3). The Alberta Provincial Thoracic Tumour Team recommends that this dose be between 10 and 15 Gy in 5-10 fractions, depending on individual patient circumstances.

Palliative Therapy

In patients where lung reserve or effusion precludes radical radiotherapy, palliative chemotherapy and/or palliative radiotherapy are the recommended treatment options. Palliative chemotherapy options for stage III and stage IV NSCLC patients with a superior sulcus tumour are similar: a platinum-based doublet for first line treatment followed by docetaxel, erlotinib, or pemetrexed for subsequent treatment as necessary.

As stated in the CCO guideline for unresected stage III NSCLC, insufficient evidence exists to determine the optimal dose or timing of radiotherapy when the goal of therapy is symptom palliation.[10] Reasonable treatment options may include: 20 Gy in 5 fractions, 30 Gy in 10 fractions, 18 Gy in 3 fractions, or 36-39 Gy in 12-13 fractions. Decreased survival and quality of life were associated with single-fraction 10 Gy radiotherapy when compared to 20 Gy in 5 fractions in one multi-centre Canadian clinical trial, therefore this regimen is not recommended.[11] However, the Alberta Provincial Thoracic Tumour Team members agree with the CCO consensus that single fractions of radiotherapy less than 10 Gy may be appropriate in some clinical circumstances, such as poor performance status or patient travel distance (recommendation #7).

TREATMENT ALGORITHM



GLOSSARY OF ABBREVIATIONS

Acronym	Description
CCO	Cancer Care Ontario
ECOG	Eastern Cooperative Oncology Group
IASLC	International Association for the Study of Lung Cancer
JCOG	Japan Clinical Oncology Group
NSCLC	non-small cell lung cancer
RR	relative risk
SCLC	small cell lung cancer
SWOG	Southwest Oncology Group
TNM	tumour-node-metastasis

DISSEMINATION

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

EVALUATION STRATEGY

A formal review of the guideline will be conducted at the Annual Provincial Meeting in 2013. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

DECLARATION OF CONFLICT OF INTEREST

Participation of members of the Alberta Provincial Thoracic Malignancies Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Thoracic Malignancies Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

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