NON-SMALL CELL LUNG CANCER
STAGE III

Effective Date: April, 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).[3] The staging definitions and stage groups for NSCLC are summarized in a supporting document (NSCLC Staging System).

GUIDELINE QUESTIONS

1. What are the recommended treatment options for patients with operable stage III non-small cell lung cancer?
2. What are the recommended treatment options with curative intent for patients with inoperable stage III non-small cell lung cancer?
3. When is palliation recommended, and what are the recommended palliative treatment options for patients with inoperable stage III non-small cell lung cancer?

DEVELOPMENT AND REVISION HISTORY

This guideline was reviewed and endorsed by the Alberta Provincial Thoracic Tumour Team. Members of the Alberta Provincial Thoracic 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. It was revised in September, 2009 and April, 2012.

SEARCH STRATEGY

For this guideline update, the working group conducted a search for new or updated practice guidelines published since September 2009 by accessing the websites of the following organizations: Cancer Care Ontario, the British Columbia Cancer Agency, Cancer Care Nova Scotia, the National Comprehensive Cancer Network, the American Society of Clinical Oncology, the Scottish Intercollegiate Guidelines

Network, the National Institute of Health and Clinical Excellence, the American College of Chest Physicians, the European Society of Medical Oncology, Irish Journal of Oncology and Cancer Council Australia.

Medical journal articles were searched using the Medline, Cochrane Database of Systemic Reviews, and PubMed electronic databases. The search term “non small cell lung cancer stage III” was searched, including related terms. Limits placed on the search included: publication between 2008 and present, “meta-analysis”, “clinical trial”, “randomized controlled trial”, “clinical trial, phase III”, “clinical trial, phase IV”, “controlled clinical trial”, “humans”, and “English”. Results were further excluded if they were phase I or II clinical trials, included less than 100 patients with stage III non-small cell lung cancer (in clinical trials), were not related to treatment, focused only on the treatment of metastases, did not include an analysis of outcomes achieved by patients with stage III disease and did not discuss survival. The reference lists of relevant Cochrane reviews and guidelines by ACCP and NCCN were scanned to further identify relevant phase III clinical trials.

The working group reviewed the acceptability and findings of all relevant literature and updated the guideline for the treatment of stage III non-small cell lung cancer. A draft of the guideline was then circulated to the entire provincial tumour team for final feedback and approval.

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.

Treatment for Operable Disease (T3N1, selected T4N0-1)

2. Surgical resection is recommended.
3. Extended pulmonary resection may be performed in selected lesions. These include peripheral lesions invading the chest wall, apical lung carcinomas, central lesions with limited mediastinal invasion, or focal pericardial or phrenic nerve invasion. Carinal tumours and those within 2 cm of the carina occasionally may be amenable to resection with airway reconstruction.
4. Platinum-based chemotherapy regimens are recommended as post-operative adjuvant therapy in the management of patients with completely resected stage IIIA NSCLC.
   - Cisplatin-based treatment is preferred, although carboplatin-based regimens can be used as an alternative if there is a contraindication to cisplatin.
5. Adjuvant radiotherapy after surgical resection is not routinely recommended. However, this treatment could be considered when there is microscopic involvement of the resection margin, including the bronchial resection margin.

Curative Intent Treatment for Inoperable Disease

6. Combined concurrent chemo-radiation is recommended for inoperable stage III 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 of 55Gy in 25 fractions to 66Gy in 33 fractions is the recommended treatment option.

7. For patients with borderline performance status or moderate weight loss (5-10%), concurrent or sequential chemo-radiation or higher dose hypofractionated radiation are options.

Treatment for T1-3N2 Disease

8. Concurrent chemo-radiation is recommended for pre-operatively diagnosed N2 disease. Cisplatin-based chemotherapy (with either etoposide or vinorelbine) and thoracic radiation of 55 Gy in 25 fractions to 66 Gy in 33 fractions is the recommended treatment option. Additional cycles of chemotherapy can be considered for bulky disease.
9. In select patients, neoadjuvant chemoradiotherapy followed by lobectomy can be considered. Pre-operative pathologically diagnosed N2 disease is not recommended to undergo surgical resection alone.
10. For patients with N2 disease discovered intra-operatively where complete resection of the lymph nodes and primary tumour is technically possible, completion of the planned lung resection is recommended.
11. In patients with N2 disease discovered intra-operatively, platinum-based adjuvant chemotherapy is recommended. Adjuvant radiotherapy can be considered in select patients.

Palliative Treatment for Inoperable Disease

12. In patients where lung reserve precludes radical radiotherapy, palliative chemotherapy and/or palliative radiotherapy are recommended.
13. Palliative chemotherapy options include:
- 1st line: platinum-based doublets
- 2nd line: docetaxel, erlotinib or pemetrexed

14. For symptomatic patients with poor performance status (ECOG>2) and/or significant weight loss (usually defined as >10% in previous 3 months), radiotherapy for symptom palliation is recommended. Dose-fractionation schedule options include:
- 20Gy in 5 fractions or 30Gy in 10 fractions
- Single fractions of radiotherapy less than 10Gy may be appropriate in some clinical circumstances such as poor performance status or patient travel distance.
- Split course radiation can also be used in select cases.

For more information, please see the Non-Small Cell Lung Cancer, Stage IV Guideline.

Follow up and Surveillance

15. Although there is no high level evidence, expert opinion recommends that a CT scan be administered 3-6 months post-treatment.
16. Follow-up appointments are recommended every 6 months for the next 2 years. Chest x-ray or CT can be used for scans following the first appointment.

DISCUSSION

Treatment for Operable Disease (T3N1, selected T4N0-1)

Surgery remains the most commonly recommended option for treating patients with medically operable NSCLC. The British Columbia Cancer Agency (BCCA), National Comprehensive Cancer Network (NCCN) and American College of Chest Physicians (ACCP) recommend for its use for stage T3N1, T4N0-1 disease.[4-6]

A Cochrane meta-analysis (2010) found that mediastinal lymph node dissection appears to improve survival compared with lymph node sampling in patients with stage IIIA NSCLC, but the strength of this evidence is limited by the small number of participants studied to date.[7] The Alberta Thoracic Tumour Team recommends that surgical resection be undertaken in those patients who are medically and surgically operable prior to the initiation of any other treatment (recommendations #2-3).

Platinum-based chemotherapy regimens are recommended as post-operative adjuvant therapy in the management of patients with completely resected stage IIIA NSCLC (recommendation #4). The benefit of adjuvant cisplatin-based chemotherapy has been demonstrated consistently by phase III clinical trials and meta-analyses using data from these trials. Arriagada et al.(2004) randomly assigned 1867 patients who had a complete surgical resection to either 3-4 cycles of cisplatin-etoposide, cisplatin-vinorelbine, cisplatin-vinblastine, cisplatin-vindesine or observation. A total of 39.3% of patients had stage III NSCLC. Patients in the chemotherapy arm, regardless of regimen, had significantly higher 5 year overall survival rates (44.5% vs. 40.4%, $p<0.03$), and significantly higher 5 year disease-free survival rate (39.4% vs. 34.3%, $p<0.003$).[8] In a long term analysis published in 2010 after 7.5 year of follow-up, differences were observed in overall survival before and after five years of follow-up (HR 0.86; 95% CI 0.76-0.97 p=0.01 versus HR 1.45; 95% CI 1.02-2.07 p=0.06). Though the results continue to favour chemotherapy, they do not as strongly at 7.5 as they did at 5 years.[9]

Another phase III study of 799 patients with completely resected NSCLC, 39% of which had IIIA stage disease post-operatively, randomly assigned patients to either an observation group or cisplatin-vinorelbine and post-operative radiotherapy in certain cases. The HR for overall survival favoured adjuvant chemotherapy (HR 0.80; 0.66-0.96, p=0.017). The overall survival with chemotherapy at 5 years improved by 8.6% compared with observation, and this improvement was maintained at 7 years (8.4%). Disease-free survival also favoured chemotherapy (HR 0.76; 95%CI 0.64-0.91).[10] A meta-analysis of 1888 patients from 4 studies evaluated the impact of adjuvant cisplatin-vinorelbine versus observation in completely resected NSCLC. Survival improvement at 5 years was 8.9% with cisplatin-vinorelbine versus observation (HR 0.80; 95% CI0.70-0.91, $p<0.001$). The analysis found stage to be an important predictor of survival at 5 years, with stage III disease having the highest benefit from chemotherapy (14.7%) versus observation.[11]

In terms of which combinations of cisplatin-based chemotherapy are most effective as adjuvant therapy for completely resected NSCLC, a meta-analysis by Pignon et al. (2008) found that the effectiveness of chemotherapy did not vary significantly with either vinorelbine, etoposide or vinca alkaloid (test for interaction, p=0.11).[12] This meta-analysis looked at data from the five largest trials since 1995 of cisplatin-based chemotherapy versus observation in 4584 completely resected patients with NSCLC by the LACE collaborative group. Their analysis also demonstrated that the effect of chemotherapy was more significant in patients with better WHO Performance Statuses (PS) (test for trend, p=0.009 for OS and p=0.01 for DFS), but data on PS was not available for all trials analyzed.

Adjuvant radiotherapy after surgical resection is not routinely recommended (recommendation #5). However, this treatment could be considered when there is microscopic involvement of the resection margin, including the bronchial resection margin. The Post-Operative Radiotherapy (PORT) Meta-analysis Trialists Group (2010) found evidence that post-operative radiotherapy in patients with completely resected NSCLC had a detrimental effect on overall survival. An exploratory analysis by stage and nodal status suggested that this effect was more pronounced in earlier stage patients and those with lower nodal status. Considering the results for stage III patients by themselves, there was no clear evidence of a detrimental effect of PORT (trend across all stages p=0.004).[13]

Curative Intent Treatment for Inoperable Disease

A seven year follow-up of the CALGB 8433 trial, which compared cisplatin-vinblastine followed by radiotherapy with radiotherapy alone, demonstrated a continued survival advantage among those patients who underwent sequential chemoradiotherapy.[14] Their median survival time was significantly greater (13.7 months) than that of the patients who only received radiotherapy (9.6 months, p=0.012). At seven years, 13 patients were still alive from the CT-RT group, whereas only six from the RT only group survived.[14]

Clinical trials and meta-analyses have since shown that concurrent chemoradiotherapy results in better survival outcomes than sequential. A meta-analysis by O'Rouke et al. (2010) demonstrated a 10% benefit in 2 year survival for concurrent versus sequential chemoradiation. An 8% reduction in risk for concurrent chemoradiation compared with radiotherapy alone and a 13% reduction in risk with concurrent versus sequential radiation was observed.[15] Nevertheless, more treatment-related deaths (4% versus 2%) were reported in the concurrent arm, though this outcome was not statistically significant. An increase in severe esophagitis could also be seen within the concurrent treatment arm. Auperin et al. (2010) also observed a significant benefit of concurrent chemoradiotherapy (HR 0.84; p=0.004) as compared with sequential, with an absolute survival benefit of 5.7% at 3 years, increasing survival from 18.1% in the sequential arm to 23.8% in the concurrent arm.[16] However, the increase in esophageal toxicity (Grade 3-4) was significant when comparing sequential with concurrent chemoradiotherapy (4% versus 18%).

A phase III study by Furuse et al. (1999) of 323 patients compared a cisplatin, vindestine, mitomycin regimen and concurrent RT versus RT sequentially delivered after the same CT regimen. The response rate for the concurrent arm was significantly higher than the sequential arm (84% versus 66%, p=0.0002). Furthermore, the median survival duration was significantly longer among those patients who received concurrent chemoradiotherapy (16.5 months versus 13.3 months, p=0.039). In terms of toxicity, myelosuppression was significantly greater among patients in the concurrent arm (p=0.0001).[17] Based on this evidence, the Alberta Thoracic Tumour team recommends the use of concurrent chemoradiation for inoperable stage III 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 (recommendation #6). For patients with borderline performance status or moderate weight loss (5-10%), concurrent or sequential chemoradiation or higher dose hypofractionated radiation are options (recommendation #7).

Cisplatin-based chemotherapy (with either etoposide or vinorelbine) and thoracic radiotherapy of 55 Gy in 25 fractions to 66 Gy in 33 fractions is the recommended treatment option. Additional cycles of chemotherapy can be considered for bulky disease (recommendation #8). Yamamoto et al. (2010) conducted a three-armed trial comparing concurrent mitomycin-vindestine-cisplatin and RT with concurrent irinotecan-carboplatin and RT and concurrent paclitaxel-carboplatin and RT, each followed by

consolidation chemotherapy. No significant difference in overall survival or progression-free survival was observed between the three groups. However, grade 3 or greater hematologic and gastrointestinal toxicity and incidence of infection and febrile neutropenia were significantly higher in the mitomycin-vindestine-cisplatin arm.[18] Carboplatin/ paclitaxel did not reach non-inferiority, but was better tolerated, and can be considered as an alternative to cisplatin/etoposide or vinorelbine.[18] Another phase III trial compared concurrent docetaxel-cisplatin and RT with concurrent mitomycin-vindestine-cisplatin and RT.[19] No significant ($p>0.05$) difference was observed in the response rate, 2-year survival rate, and median survival between the docetaxel-cisplatin (78.8%, 60.3% and 26.8 months, respectively) and the mitomycin-vindestine-cisplatin (70.3%, 48.1% and 23.7 months, respectively) arms.[19]

Bradley et al. (2011) reported findings from the interim analysis of the RTOG 0617 trial comparing the overall survival of patients treated with high-dose (74Gy) versus standard dose (60Gy) radiotherapy with concurrent chemotherapy +/- cetuximab (400mg/m^2).[20] Concurrent chemotherapy included weekly paclitaxel (45mg/m^2) and carboplatin (AUC=2). The preliminary results of the study demonstrate that high dose radiation as delivered in this trial, does not improve survival outcomes (1 year OS rate 70.4% versus 81% in the low dose arm).[21] The high-dose radiation arm of this trial has been closed following these findings.[20]

A meta-analysis by Delbaldo et al. (2007) of the Cochrane Lung Cancer Group investigated the impact of adding another drug to a single-agent or double-agent chemotherapy regimen for non-small cell lung cancer patients with advanced disease.[22] The pooled analysis demonstrated that a significant increase in tumour response (OR 0.42; 95%CI 0.37-0.47, $p<0.001$) and one year survival (OR 0.80; 95% CI 0.70-0.91, $p<0.001$) occurred when comparing the single-agent with doublet regimens. When comparing the doublet and triplet regimens, the odds ratio favoured the triplet (OR 0.66, 95% CI 0.58-0.75, $p<0.001$), but not one-year survival in which the difference was not significant (OR 1.01, 95% CI 0.85-1.21, $p=0.88$).[22]

Treatment for T1-3N2 Disease

Concurrent chemo-radiation is recommended for unresected N2 disease. Cisplatin-based chemotherapy (with either etoposide or vinorelbine) and thoracic radiation of 55Gy in 25 fractions to 66Gy in 33 fractions is the recommended treatment option (recommendation #8). Please see the discussion in section **Curative Intent Treatment for Inorperable Disease** for evidence also pertaining to IIIA N2 disease.

In select patients, neoadjuvant chemoradiotherapy followed by lobectomy can be considered. Pre-operative pathologically diagnosed N2 disease is not recommended to undergo surgical resection alone (recommendation #9). Thomas et al. (2008) compared pre-operative chemotherapy with pre-operative chemo-radiotherapy in patients with stage IIIA-B NSCLC with invasive mediastinal assessments. In the patients who underwent complete resection, the proportion of those with mediastinal downstaging (46% versus 29%, $p=0.02$) and pathological response (60% versus 20%, $p<0.0001$) favoured the chemo-radiotherapy arm.[23] A retrospective study by Higgins et al. (2009) of pre-operative chemotherapy versus pre-operative chemo-radiotherapy in stage IIIA N2 patients resulted in a similar outcome. The mediastinal complete pathological response in the chemoradiotherapy group was 65%, versus 35% in the preoperative chemotherapy alone group.[24] However, in both of these studies, survival outcomes were not significantly different between the two groups.

Johnstone et al. (2002) compared induction chemotherapy (cisplatin, vinblastine and mitomycin-C) and surgery with the same induction chemotherapy regimen and radiotherapy. Both groups received additional chemotherapy that consisted of cisplatin and vinblastine. No difference between the surgery and RT

groups was observed in terms of the one year survival rate (70% vs. 66%, respectively) or median survival time (19.4 months vs. 17.4 months, respectively). However, due to the lower than expected accrual of patients in this trial, no definitive conclusions can be made. A similar trial was conducted by Van Meerbeeck et al. (2007) with resulting OS and PFS similar in both groups.[25] In this study, induction chemotherapy resulted in a response rate of 61%, and a total of 167 patients were randomized to the surgery arm, and 165 to radiotherapy. The authors conclude that radiotherapy should be considered the preferred locoregional treatment for these patients.

Albain et al. (2009) conducted a phase III trial comparing concurrent cisplatin-etoposide and radiotherapy followed by surgery with concurrent cisplatin-etoposide and radiotherapy followed by radiotherapy. Both groups received two additional cycles of cisplatin-etoposide. No significant difference was observed in terms of overall survival between the groups in their study that underwent resection and those who underwent an extra course of radiotherapy (23.5 months versus 22.2 months), however, median progression free survival was longer (12.8 months versus 10.5 months, respectively).[26] A matching analysis for four pre-study factors for group 1 against group 2 subsets was feasible, and the rate of overall survival was improved in the surgical group if a lobectomy was done (median 33.6 months versus 21.7 months in the CT-RT group), but not a pneumonectomy, compared with the rate in the matched chemo-radiotherapy group.[26]

In patients with NSCLC who have incidental (occult) N2 disease found at surgical resection and in whom complete resection of the lymph nodes and primary tumour is technically possible, completion of the planned lung resection is recommended (recommendation #10).

In patients with N2 disease discovered intra-operatively, platinum-based adjuvant chemotherapy is recommended. Adjuvant radiotherapy can be considered in select patients (recommendation #11). Consideration can be given for subsequent cycles of chemotherapy, excluding docetaxel. The same chemotherapy as was administered previously is recommended. The PORT meta-analysis (2010) determined that there is no clear evidence of a detriment or benefit from post-operative radiotherapy alone in terms of survival among patients with stage IIIA, N2 disease as compared with surgery alone.[13] Douillard et al. (2006) studied the impact of adjuvant cisplatin-vinorelbine versus observation in patients with completely resected stage I, II or IIIA disease in their prospective, randomized phase III trial.[10] The five year overall survival rate in patients with N2 disease was 40% for the adjuvant chemotherapy arm versus 19% in the observation arm. The addition of post-operative radiotherapy was recommended for patients in the trial with pathological node positive disease but was not mandatory and patients were not randomized to it. For patients given PORT, treatment was initiated either 2 weeks after their last chemotherapy treatment or 2 weeks after randomization to the observation arm. Patients with N2 disease treated with PORT in the cisplatin-vinorelbine arm had a median overall survival of 47.7 months versus 23.8 months in those treated with CT but not PORT. In the observation arm, the median overall survival for those treated with PORT was also higher, at 22.7 months versus 12.7 months.[27] The CALGB 9734 trial in which patients with N2 disease were randomized to adjuvant carboplatin/paclitaxel with or without radiotherapy found that post-operative RT did not improve one-year overall survival (72% versus 74% for no RT).[28]

Wisnivesky et al. (2012) compared the survival of elderly patients who received PORT with those who did not using the Surveillance, Epidemiology, and End Result (SEER) registry linked to Medicare records.[29] The data suggests that PORT alone is not associated with improved survival in elderly patients with N2 disease (HR=1.11, 95% CI 0.97-1.27).[29]

Palliative Treatment for Inoperable Disease

In patients where lung reserve precludes radical radiotherapy, palliative chemotherapy and/or palliative radiotherapy are recommended. Palliative chemotherapy options include as first line platinum-based doublets and as second line docetaxel, erlotinib or pemetrexed (recommendation #12-13).

For symptomatic patients with poor performance status (ECOG>2) and/or significant weight loss (usually defined as >10% in previous 3 months), radiotherapy for symptom palliation is recommended (recommendation #14). Dose-fractionation schedule options include 20Gy in 5 fractions or 30Gy in 10 fractions. Single fractions of radiotherapy less than 10Gy may be appropriate in some clinical circumstances such as poor performance status or patient travel distance. Split course radiation can also be used in select cases. This recommendation is in line with the most recent *Consensus Statement on Palliative Lung Radiotherapy*.[30]

There is some debate as to which radiotherapy regimen is the most beneficial and least toxic for patients with locally advanced or metastatic NSCLC who are not suitable for curative-intent radical radiotherapy. In a recent Cochrane review, Lester et al. reviewed 14 randomized controlled trials and reported that no single regimen was superior in terms of palliation of symptoms.[31] The same was reported in the systematic review by Okawa et al. (2006) of Cancer Care Ontario's Program in Evidence-Based Care.[32]

Although none of the studies reviewed by Lester et al. reported a significant increase in survival, higher dose palliative radiotherapy was associated with more frequent reports of toxicity and visits to the hospital. Lester et al. concluded that in patients with a poor PS (3-4), short courses of palliative radiotherapy, such as 10 Gy in one fraction or 16-17 Gy in two fractions, were better tolerated. The most frequently reported and serious adverse effect was radiation myelitis, therefore they stressed that care should be taken to either avoid irradiating or reduce the dose to the spinal cord if the 17 Gy/2 fractions dose was used.[31] In patients with a good PS (0-1), the authors also concluded that higher dose palliative regimens, such as 36 Gy in 12 fractions, could be considered.[31] In the systematic review and meta-analysis performed by Fairchild et al., data from 13 randomized controlled trials was analyzed. Doses of palliative RT ≥35Gy in 12 fractions were found to be predictive of improvements in overall survival compared to lower dose RT (26.5% versus 21.7% at 1 year, p=.002).[33]

EGFR Inhibitors

A phase III trial comparing maintenance gefitinib, an epidermal growth factor receptor (EGFR) inhibitor, with observation also demonstrated no clinical benefit to its use in patients with inoperable stage III NSCLC.[34] Patients in this trial received cisplatin-etoposide concurrently with radiotherapy, followed by three cycles of docetaxel. If they experienced no disease progression, they were randomly assigned to gefitinib or a placebo until disease progression, toxicity or the end of 5 years. The trial was closed at an interim analysis due to the lack of improvement in survival among those patients taking gefitinib. Median survival time was 23 months for gefitinib (n=118) and 35 months for the placebo (n=125) at a median follow-up of 27 months.[34]

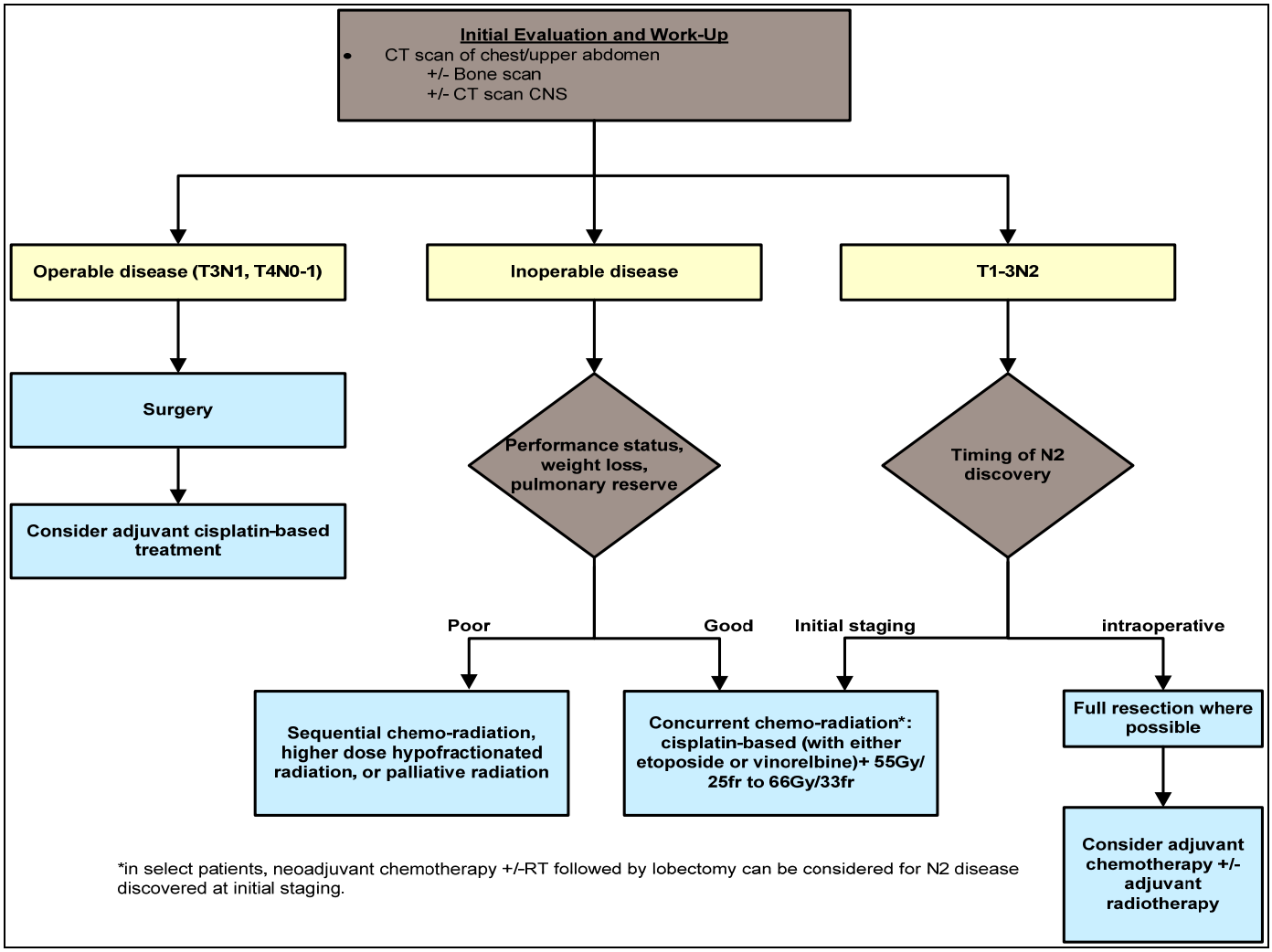
Follow up and Surveillance

The value of follow-up in lung cancer includes monitoring treatment complications, gauging the outcomes of treatment, detection of relapses and recurrence, provision of information, supportive and palliative care.[35] Although there is no high level evidence, expert opinion recommends that a CT scan be

administered 3-6 months post-treatment (recommendation #15). Follow-up appointments are thereafter recommended every 6 months for the next 2 years. Chest x-ray or CT can be used for scans following the first appointment (recommendation #16). There is little agreement among published guidelines regarding the ideal follow-up strategy, and little research has been done on this topic.[4,6,35,36]

A systematic review by Schmidt-Hansen et al. (2012) concludes that the current available studies of follow-up are marked by methodological issues, and it is not possible to make any firm recommendations about the most effective follow-up strategy.[35]

TREATMENT ALGORITHM



GLOSSARY OF ABBREVIATIONS

Acronym	Description
CT	Chemotherapy
HR	Hazard ratio
LACE	Lung Adjuvant Cisplatin Evaluation
NSCLC	Non-small cell lung cancer
OS	Overall survival
PFS	Progression-free survival
PORT	Post-operative radiotherapy
PS	Performance status
RT	Radiotherapy
SCLC	Small cell lung cancer

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 Alberta Health Services, Cancer Care.

MAINTENANCE

A formal review of the guideline will be conducted at the Annual Provincial Meeting in 2012. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

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. Alberta Health Services – Cancer Care 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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