Guideline Resource Unit
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# Unresectable Stage III Non-Small Cell Lung Cancer

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Cancer Care Alberta

Clinical Practice Guideline LU-015 – Version 1
www.ahs.ca/guru

## Background

Lung cancer is the overall leading cause of cancer mortality in Canadian men and women. By the end of 2024, an estimated 20,700 Canadians have died lung cancer.[1] In addition, more Canadian men and women will die from lung cancer as compared to prostate, breast, and colorectal cancers combined. In 2024, the latest year for which statistics are available, lung cancer was the leading cause of cancer death for both men and women in Alberta.[2] Smoking remains the most important risk factor for lung cancer. According to the Canadian Tobacco and Nicotine Survey in 2022, 10.9% of Canadians and 12.0% of Albertans smoke.[3] In males, the incidence of lung cancer began to level off in the mid-1980s and has since been declining, whereas in females, the incidence of lung cancer didn't stop increasing until 2006. The differences in lung cancer incidence among males and females likely reflect past changes in tobacco use. In males, a drop in smoking began in the mid-1960s, preceding the drop in lung cancer incidence by almost 20 years. In females, tobacco consumption didn't begin to drop until the mid-1980s, suggesting that lung cancer incidence rates in women should begin to decrease in the next two decades. Despite much research and many clinical advances in lung cancer treatments, the age-standardized five-year survival rate for all types and stages of lung cancer combined is only 22% for Canada overall, and 22% for Alberta.[4]

Lung cancer can be classified into non-small cell lung cancer (NSCLC) or small-cell lung cancer (SCLC). NSCLC accounts for 80% of all lung cancer cases and is categorized using the TNM staging system. The majority of tumors found in stage 3 NSCLC are determined to be unresectable, which means the cancer cannot be removed with surgery.

## Guideline Questions

1. What is the appropriate workup for patients with suspected unresectable stage III NSCLC?
2. What is the appropriate management of patients with unresectable NSCLC?

## Target Population

The following recommendations apply to adults over the age of 18 years with suspected unresectable stage III NSCLC.

## Recommendations

Whenever possible, patients should be considered for eligibility in ongoing clinical trials. Up-to-date information on trials offered in Alberta is available on the Alberta Cancer Clinical Trials website.

**Diagnosis**

1. CT scan of the chest and FDG-PET are required.
2. Consider imaging of the brain if neurological symptoms, with contrast-enhanced MRI or CT, depending on availability. MRI is preferred.

3. If PET is negative for distant metastases, mediastinal staging is required either by endobronchial ultrasound or mediastinoscopy.[5]
4. PD-L1 IHC expression alongside EGFR and ALK status is required to help individualize treatment decision making.

**Management**

5. In patients with adequate organ function, performance status and no contraindications to chemotherapy or radical radiation therapy, unresectable stage III NSCLC should be treated with concurrent chemoradiation with platinum-doublet chemotherapy.[6, 7] Carboplatin/cisplatin with etoposide, pemetrexed, vinorelbine or paclitaxel are reasonable options for adenocarcinoma histology.[8-10] Carboplatin/cisplatin with etoposide, vinorelbine or paclitaxel are reasonable options for squamous histology.
6. For concurrent chemoradiation, 60-66 Gy is recommended for definitive treatment (for Pancoast tumours, 45 Gy in 25 fractions in patients undergoing planned trimodality treatment).[11-13]
7. Patients with stage III NSCLC (without an EGFR or ALK mutation) who have completed concurrent chemoradiation without evidence of disease progression should be offered consolidation durvalumab for up to 12 months or consider clinical trial.[14] Durvalumab can only be offered to patients without any contraindications to immunotherapy with adequate organ function and performance status.
8. In patients with an EGFR exon 19 deletion or exon 21 L858R mutation, treatment with osimertinib after definitive chemoradiotherapy had a significantly improved median progression-free survival (PFS) of 39.1 months versus 5.6 months with placebo (PFS hazard ratio of 0.16, 95% confidence interval [CI], 0.10 to 0.24; P<0.001). Thus, patients with unresectable stage III NSCLC with an EGFR exon 19 deletion or exon 21 L858R mutation who have completed concurrent chemoradiation without evidence of disease progression may be offered osimertinib until disease progression, if accessible, or consider clinical trial.[15]
9. There is insufficient data to recommend consolidation therapy in patients with ALK-mutated unresectable NSCLC. Clinical trials should be considered, if available.

**Special Populations:**

10. ECOG≥2 and/or patients with multiple comorbidities: Patients with unresectable stage III NSCLC who are not candidates for radical radiation can be considered for palliative radiation. Evolving data also suggests a benefit of local consolidative radiotherapy in patients with oligometastatic disease to all disease sites.

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## Development and Revision History

This guideline was developed by a multidisciplinary working group comprised of members from the Alberta Provincial Lung Tumour Team and a methodologist from the Guideline Resource Unit. The draft guideline was externally reviewed and endorsed by members of the Alberta Provincial Lung Tumour Team who were not involved in the guideline's development, including surgical oncologists, radiation oncologists, medical oncologists, nurses, pathologists, and pharmacists. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in 2025.

## Maintenance

A formal review of the guideline will be conducted in 2030 If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

## Abbreviations

AHS, Alberta Health Services; ALK, anaplastic lymphoma kinase; CCA, Cancer Care Alberta; CI, confidence interval; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; FDG, fluorodeoxyglucose; Gy, Gray; IHC, immunohistochemistry; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; PET, positron emission tomography; PFS, progression free survival; SCLC, small cell lung cancer; TNM, tumor, node, metastasis.

## Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Lung Tumour Team and are a 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.




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All cancer drugs described in the guidelines are funded in accordance with the Outpatient Cancer Drug Benefit Program, at no charge, to eligible residents of Alberta, unless otherwise explicitly stated. For a complete list of funded drugs, specific indications, and approved prescribers, please refer to the *Outpatient Cancer Drug Benefit Program Master List*.


## Conflict of Interest Statements

***Dr. Doreen Ezeife**, medical oncologist, reports receiving honoraria from Pfizer, Bristol Myers Squibb, and Novartis, and is a member of the advisory board for Pfizer and Novartis.
**Dr. Quincy Chu,** medical oncologist, reports receiving grants and/or contracts from Astra Zeneca; consulting fees from Abbvie, Amgen, AnHeart, Astellas, Astra Zeneca, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, Genprex, GSK, Janssen, Merck and Co, Novartis, Ocellaris, Pfizer, Roche, and Takeda; honoraria from Astra Zeneca, Daiichi Sankyo, Roche, and Abbvie; participates on data safety monitoring board or advisory board at Abbvie, Amgen, AnHeart, Astellas, Astra Zeneca, Boehringer Ingelheim, Bristol Myer Squibb, Daiichi Sankyo, Eli Lilly, Genprex, GSK, Janssen, Merck and Co, Novartis, Ocellaris, Pfizer, Roche, and Takeda; and has a leadership or fiduciary role at Lung Cancer Canada, and Canadian Mesothelioma Foundation.
**Dr. Zsolt Gabos**, radiation oncologist, has nothing to disclose.
**Teresa Ruston**, nurse practitioner, has nothing to disclose.
**Ellen de Jong, PhD,** methodologist, has nothing to disclose.

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