Lung Cancer Treatment Guidelines

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Derived and updated by consensus of members of the Providence Thoracic Oncology Program with the aid of evidence-based National Comprehensive Cancer Network (NCCN) national guidelines, American Society of Clinical Oncology (ASCO) and National Guidelines Clearing House.

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TNM Staging

Clinical Trials
Lung Cancer Treatment Guidelines

General Principles

- The multidisciplinary management of patients with lung cancer is crucial. Collaborative involvement of multiple specialties with different areas of expertise in the care of the patient with lung cancer is an essential component of state of the art management of all stages of lung cancer.
- All lung cancer patients with greater than stage IA resected disease or those with complex management questions should be reviewed in a multidisciplinary thoracic disease conference with subsequent recommendations communicated to the referring and participating physicians and patient.
- All eligible patients should be offered participation in clinical trials.
- All patients being considered for resection with mediastinal nodes \( \geq 1 \) cm or radiographically suspicious on CT scan and/or PET, must undergo pathologic staging of the mediastinum prior to resection of the primary tumor.
- Patients with small, positive N2 nodes should be evaluated in a multidisciplinary setting for surgical resectability. If patients are felt to have surgically resectable disease, they should be entered into clinical trials or undergo preoperative chemotherapeutic and/or radiation therapy prior to resection. If unresectable or inoperable (the majority of patients), they should be treated with chemoradiotherapy with curative intent if comorbidities allow.
- Patients with multiple or bulky, biopsy-proven mediastinal lymph node involvement are generally considered unresectable and should be treated with chemoradiotherapy with curative intent if the patient’s status is appropriate.
- All patients with centrally located tumors or T3 tumors must undergo pathologic staging of the mediastinum prior to resection, regardless of the presence or absence of suspicious nodes in the mediastinum on CT scan and/or PET.
- Smoking cessation should be advocated with all actively smoking patients, regardless of disease stage.
- For all patients with incurable disease or disease with very high risk of recurrence (locally advanced NSCLC undergoing chemotherapy, small cell lung cancer), refer to Providence Oncology Palliative Care clinic is recommended.
- Nonsquamous NSCLC not undergoing curative resection (outside of clinical trial setting) should have tissue tested for EGFR, KRAS mutations, ALK, and ROS-1 rearrangements.
- For those patients who have completed active treatment and are not appropriate candidates for Palliative Care, referral to Cancer Survivor Clinic is recommended.

Evaluation

- All suspected lung cancer patients should have a CT scan of the chest through the liver and adrenals with contrast (unless contraindicated) and laboratory tests including a blood count, chemistries, liver function tests and serum calcium.
- Evaluation of patients with other than clinical T1N0 lesions should include biopsy prior to resection when feasible. Biopsy can be accomplished by CT-guided biopsy, bronchoscopy, endobronchial- or endoscopic ultrasound guided biopsy, or mediastinoscopy or thoracic surgical procedure. The selection of techniques will depend on the location and presentation of the tumor as well as the clinical status of the patient. The goal of biopsy should be to obtain adequate tissue specimens to allow for histologic evaluation, immunohistochemical staining, and tumor mutation analysis studies whenever safe and feasible.
- Patients with abnormal alkaline phosphatase, serum calcium or bony pain should undergo bone scan or PET scan.
- Patients with neurologic symptoms, those with small cell lung cancer, or advanced stage NSCLC \( \geq II \) should undergo CNS imaging with MRI of the brain preferred unless contraindicated.
- Patients being considered for surgery should undergo complete pulmonary physiologic evaluation, cardiac risk assessment and PET evaluation prior to surgery.
- Patients undergoing definitive chemoradiation should have PET scan evaluation prior to initiating therapy.
- Anatomic resection consisting of lobectomy is preferred. If less than lobectomy is performed prefer anatomic segmentectomy to wide local excision (wedge resection). Each should be accompanied by thoracic lymphadenectomy. Sleeve resection is preferred to pneumonectomy, if technically feasible. All resected patients with greater than stage IA disease should be presented at the Multidisciplinary Thoracic Disease Conference for discussion regarding adjuvant therapy. Consultation may be considered preoperatively to assess clinical trial eligibility. For stage IA disease, patients should be considered for adjuvant chemotherapy in a clinical trial.
Non-small Cell Lung Cancer

T1N0M0:
- Consider clinical trial participation.
- Resection after negative mediastinal node dissection.
- Refer for postoperative adjuvant chemotherapy or chemoprevention studies, if available.
- Definitive radiation therapy, if medically inoperable or if patient declines surgical resection. Definitive radiation should use stereotactic body radiation (SBRT) or doses > 60 Gy if using standard (single-modality) fractionation, while respecting normal tissue tolerance.
- Refer to Cancer Survivor Clinic at the terminus of active treatment.

T2BN0M0; T1N1M0; T2N1M0
- Consider clinical trial participation.
- Resection after negative mediastinal node dissection.
- Discuss participation in adjuvant or neoadjuvant chemotherapy trials before resection if possible.
- Refer for discussion of adjuvant chemotherapy (or trials) within 3 weeks of surgery.
- Consider re-resection or adjuvant therapy (either with radiotherapy or chemoradiation, depending upon the clinical situation) for positive margins.
- For patients with N0 disease who are ineligible for or decline surgery, definitive radiation should be considered. SBRT or doses > 60 Gy with standard fractionation (while respecting normal tissue tolerance) should be employed.
- For patients with N1 disease who are ineligible for or decline surgical resection, definitive therapy with either concurrent or sequential chemoradiation should be considered.
- Refer to Cancer Survivor Clinic as appropriate.

T3N0M0
(Tumors of the superior sulcus are discussed separately below)
- Consider clinical trial participation.
- Consider induction therapy if questionably resectable due to location, chest wall involvement or PFTs. Efforts should be made to minimize time to resection after completion of induction therapy.
- Resection after prior negative mediastinal node surgical evaluation or following induction therapy.
- Refer for radiation for positive margins.
- Consider primary chemoradiation for extensive chest wall involvement.
- Consider definitive chemoradiation if medically inoperable or if patient declines surgical resection.
- Refer for discussion of adjuvant chemotherapy, on or off clinical trial, within 3 weeks of surgery.

T3N1M0, T1-3N2M0
- Consider clinical trial participation.

**Staging of the mediastinum requires biopsy.**

**ECOG performance status less than or equal to 2:**

- Non-bulky N2 nodes (resectable) - Refer for induction therapy on a clinical trial if available. If ineligible or refuses, consider therapy off protocol. Patients with positive N2 nodes after resection should be considered for adjuvant radiation therapy to the mediastinum for local control.
- All patients (N2 or otherwise) should be considered for adjuvant chemotherapy.
- Bulky N2 nodes (unresectable): consider investigational protocols or combined modality definitive therapy with chemoradiation off study if ineligible or refuses. Sequential therapy of radiation and chemotherapy should be considered for patients with marginal performance status or large tumors where normal lung toxicity would be excessive with concurrent approach.

**ECOG performance status greater than 2:**

- Radiotherapy or palliative care (including interventional airway techniques if deemed necessary for symptomatic palliation).
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- Clinical trials if available.

**T4N0-3, M0; T1-3N3M0**

*ECOG performance status less than or equal to 2:*

- Consider for clinical trials.
- Chemoradiation if clinically feasible based upon radiation treatment fields.
- Palliative single-modality chemotherapy or radiation, if not a candidate for combined-modality therapy.

*ECOG performance status greater than 2:*

- Radiotherapy or palliative care as above.
- Clinical trials if available.
- Evaluation for mutation-appropriate palliative targeted therapies.

**Tumors of the Superior Sulcus (Generally T3 or 4, N0-2), M0**

*ECOG performance status less than or equal to 2:*

- Consider for clinical trials.
- Thorough evaluation of the mediastinum for staging and prognosis.
- Thorough evaluation for surgical resectability after induction therapy. Evaluation for surgical resectability should occur rapidly after completion of induction therapy, to minimize time to completion of therapy.
- Induction chemoradiation.
- Surgical resection.
- For patients with multi-station or bulky N2 disease or who are otherwise felt to be surgically unresectable (or who decline surgery), definitive chemoradiation should be considered.

**T1-2N0-1M1 with solitary metastasis**

*ECOG performance status less than or equal to 2:*

- Thorough metastatic work-up.
- Consider metastasectomy followed by definitive treatment of the primary lesion in the context of thorough multidisciplinary review. In cases where metastasectomy might not be feasible (such as central small brain metastasis), definitive radiation may be considered.
- Consider use of stereotactic radiosurgery or surgical resection with radiation for isolated brain metastasis.
- Consider adjuvant or neoadjuvant chemotherapy or radiation depending upon pathologic findings.

**T1-4 N0-3, M1A with malignant effusion**

*ECOG performance status less than or equal to 2:*

- Chemotherapy (clinical trial or standard chemotherapy).
- Molecularly-targeted therapy as appropriate.
- Management of malignant effusion if symptomatically indicated (with indwelling home-care chest tube or pleurodesis)
- Palliative care including radiotherapy to appropriate symptomatic lesions.

*ECOG performance status greater than 2:*

- Palliative care including radiotherapy to appropriate symptomatic lesions.
- Indwelling, home-care chest tube drainage for symptomatic effusion or pleurodesis.
- Clinical trials if available.
T1-4N0-3M1A or B (except T1-2N0M1 with solitary metastasis)

ECOG performance status less than or equal to 2:

- Consider clinical trial participation.
- Chemotherapy (clinical trial or standard).
- Radiotherapy to appropriate symptomatic lesions.
- Supportive care/Palliative Care referral.
- Molecularly-targeted therapy as appropriate.

ECOG performance status greater than 2:

- Consider clinical trial participation.
- Radiotherapy to appropriate symptomatic lesions.
- Palliative care.
- Supportive care.

Synchronous primaries:

ECOG performance status less than or equal to 2:

- Thorough metastatic work-up.
- Treat for the highest stage lesion, followed by treatment for the next lesion if the highest-stage lesion is amenable to definitive therapy.

Post-Operative Follow Up

Discussion of the risks and possible benefits of surveillance imaging (for local tumor recurrence or development of second primary cancer) should be held with the patient.

Ongoing efforts of smoking cessation and tobacco abstinence should be emphasized.

Small Cell Lung Cancer

Limited stage IA (confined to one radiation field, no malignant effusion)

Resected Solitary Pulmonary Nodule

- Very limited disease defined as stage IA < 3 cm should have multidisciplinary discussion for limited resection.
- Refer for adjuvant chemotherapy.
- Consider prophylactic cranial irradiation (PCI) and clinical trial if available.

Not Resected:

- Consider clinical trial participation.
- Combined modality concurrent chemoradiation. Radiation should begin with cycle 1 or 2 of chemotherapy.
- Consider prophylactic cranial irradiation (PCI) or clinical trials for responders.

Extensive stage, including malignant effusion

- Consider clinical trial participation.
- Standard chemotherapy if ineligible or refuses.
- Consider PCI after completion of chemotherapy for patients responding to chemotherapy.
- Consider thoracic radiation for patients responding to chemotherapy.
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- Consider radiation for symptomatic metastases unresponsive to chemotherapy.
- For patients with known brain metastases, palliative whole brain radiation should be considered, with timing of radiation depending upon the patient’s clinical situation.
- Palliative Care referral.

Chemotherapy Guidelines

Adopted in review of NCCN, ASCO, Cancer Care Ontario (CCO), and European Society of Medical Oncology (ESMO) guidelines and consensus statements. The Providence Thoracic Oncology program agrees with and adopts the NCCN Guidelines as the most comprehensive and most frequently updated distillation of chemotherapy options and sequences, with the above guidelines and consensus statements noted to be in accordance with the NCCN Guidelines summary.

Specific comments or situations are included in addition:

- In the adjuvant setting, molecularly-targeted therapy, such as EGFR inhibition, regardless of mutation status, is not standard therapy off of a clinical protocol.
- In locally advanced disease for patients receiving definitive chemoradiation therapy, cisplatin-based combination therapy is the preferred choice whenever feasible.
- Tumor histology and molecular status should guide selection of chemotherapy and targeted therapy agents for NSCLC as summarized in NCCN Guidelines.
- Systemic maintenance therapy for patients with advanced disease should be considered according to NCCN guidelines and patient preference.
- Molecular mutation and gene rearrangement analyses should be performed whenever possible for advanced non-squamous NSCLC.

Oncology Palliative Care

Advanced stage lung cancer patient should be referred to Oncology Palliative Care

Physical Therapy

Physical therapy referrals are indicated when patients are having difficulty with the following: decreased endurance/ strength, cancer related fatigue, balance issues secondary to chemotherapy induced peripheral neuropathy, scar tissue restrictions, range of motion limitations, pain affecting mobility and function, gait dysfunction and assessment of assistive devices for safety in mobility.

- Refer to Physical Therapy, Occupational Therapy or Speech Therapy as appropriate.

Pain Management

Refer to Rehab for pain management as appropriate. Oncology patients with persistent pain should be referred to an oncology rehab therapist. Epic providers: submit referral to PT/OT to evaluate and treat. Note in comments: “oncology rehab therapist” (if lymphedema issue – indicate in comments). Non Epic provider should write referral on RX pad requesting PT/OT evaluate and treat for oncology therapy

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