

Recommendations Summary

Non-Small Cell Lung Cancer

Small Cell Lung Cancer

Mesothelioma

Effective Date: July, 2023



The abbreviated guideline recommendations outlined in this summary apply to adult patients with lung cancer, and are a consensus of the Alberta Provincial Lung Tumour Team. Full clinical practice guidelines with detailed descriptions of the clinical questions, recommendations, methodology, and references are under development and will be posted on the website when finalized.

Abbreviated guidelines

Perioperative management of NSCLC: neoadjuvant treatment

- Resectable stage IB to IIIA NSCLC can be treated with up to 3 cycles of neoadjuvant chemoimmunotherapy with platinum doublet with nivolumab immunotherapy¹ (Checkmate 816 data) followed by surgical resection. After surgical resection, adjuvant chemotherapy can be given for up to 4 cycles.
- EGFR and ALK positive resectable NSCLC patients should NOT receive neoadjuvant chemoimmunotherapy. These patients should receive upfront surgical resection followed by exploration of adjuvant systemic therapy (see 'Perioperative management of NSCLC: adjuvant treatment' guidelines).
- Other neoadjuvant chemoimmunotherapy regimens using durvalumab² (AEGEAN data) or pembrolizumab³ (Keynote 671 data) are also options depending on what is funded and accessible.

Perioperative management of NSCLC: adjuvant treatment

- Patients who received upfront surgical resection of resectable NSCLC can be considered for adjuvant chemotherapy if they have tumours > 3-4cm or have lymph node positive disease.
- Adjuvant chemotherapy regimens include up to 4 cycles of cisplatin-vinorelbine, or cisplatin-pemetrexed (adenocarcinoma histology only).
- Referral to radiation oncology after adjuvant chemotherapy is recommended for selected patients (e.g. margin positive resection, path stage III with multiple N2 nodes).
- PD-L1 positive ($\geq 50\%$ by SP263 assay):
 - Adjuvant atezolizumab for up to 16 cycles or 1 year should be considered after the completion of adjuvant chemotherapy⁴ (IMPOWER 010 data).
- EGFR positive:
 - Adjuvant Osimertinib for up to 3 years should be considered after the completion of adjuvant chemotherapy⁵ (ADAURA data).
 - Patients do not need to receive adjuvant chemotherapy in order to be eligible for adjuvant osimertinib. The benefit of adjuvant osimertinib is maintained irrespective of whether the patient received adjuvant chemotherapy.

Metastatic/advanced Non-small cell lung cancer (NSCLC)

- Treatment of metastatic NSCLC is driven by PD-L1 status and molecular biomarkers.
- Driver mutation negative:
 - PD-L1 \geq 50% - First-line treatment with pembrolizumab monotherapy recommended⁶ (based on the Keynote 024 data). For second-line therapy, platinum doublet chemotherapy is recommended. Third-line and subsequent options include docetaxel or erlotinib. Consider clinical trial options for fit patients.
 - Combined chemoimmunotherapy may be considered in PD-L1 high expressing disease if rapidly progressive disease/high tumour burden are present, which may preclude second line chemotherapy. Single agent anti-PD-1 and chemoimmunotherapy have not been compared directly, but meta-analyses suggest improved response rate and PFS with chemoimmunotherapy, without an overall survival advantage⁷.
 - PD-L1 $<$ 50% - First-line chemoimmunotherapy with platinum doublet and immunotherapy. Carboplatin, pemetrexed, pembrolizumab is recommended for adenocarcinoma histology⁸ (Keynote 189 data). Either carboplatin, gemcitabine, pembrolizumab or carboplatin, paclitaxel, pembrolizumab is recommended for squamous histology⁹ (Keynote 407 data)
 - Ipilimumab, nivolumab and two cycles of platinum doublet chemotherapy¹⁰ (CHECKMATE-9LA) is also an option, agnostic of PD-L1 status, in EGFR/ALK wild-type disease.
 - For second-line therapy, docetaxel is recommended. Third-line and subsequent options include erlotinib. Consider clinical trial options for fit patients.

Driver mutation positive:

- EGFR positive – First-line Osimertinib is recommended¹¹ (FLAURA data). Second-line systemic therapy options include clinical trials or platinum doublet chemotherapy, ideally including pemetrexed. Consider radiation for oligo-progressive disease. Third-line and subsequent options include docetaxel or erlotinib. Consider clinical trial options for fit patients.
- Patients with EGFR positive disease who received first/second generation EGFR tyrosine kinase inhibitors (e.g. gefitinib, erlotinib, afatinib) and have developed progressive disease may be tested for T790M by liquid biopsy or tissue biopsy. T790M+ disease should be treated with Osimertinib¹² (AURA data).
- ALK positive – First-line options include alectinib¹³ (ALEX data), lorlatinib¹⁴ (CROWN data) or brigatinib¹⁵ (ALTA-1L data). Targeted therapy is not funded in subsequent lines, and can be difficult to access. Second-line systemic therapy options include clinical trials or targeted therapy if accessible, or platinum doublet chemotherapy, ideally including pemetrexed. Consider radiation for oligoprogressive disease. Third-line and subsequent options include docetaxel or erlotinib. Consider clinical trial options for fit patients.

- ROS1 positive - First-line options include entrectinib¹⁶ or crizotinib. Targeted therapy is not funded in subsequent lines and can be difficult to access. Second-line systemic therapy options include clinical trials or targeted therapy if accessible, or platinum doublet chemotherapy. Consider radiation for oligoprogressive disease. Third-line and subsequent options include docetaxel or erlotinib. Consider clinical trial options for fit patients.
- RET positive – First-line options include selpercatinib¹⁷ (LIBRETTO data) or pralsetinib¹⁸ (ARROW data). Second-line systemic therapy options include clinical trials or platinum doublet chemotherapy. Consider radiation for oligoprogressive disease. Third-line and subsequent options include docetaxel or erlotinib. Consider clinical trial options for fit patients.
- BRAF positive – see recommendations above for driver mutation negative NSCLC. Can consider treatment with BRAF inhibitor depending on patient comorbidities, age, performance status and patient’s preferences.
- KRAS G12C positive - see recommendations above for driver mutation negative NSCLC. If accessible, can consider treatment with sotorasib or adagrasib depending on patient comorbidities, age, performance status and patient’s preferences.
- HER2 positive – see recommendations above for driver mutation negative NSCLC. If accessible, consider trastuzumab-deruxtecan depending on patient comorbidities, age, performance status and patient’s preferences. Note that this drug is not Health Canada approved or provincially reimbursed for this indication.
- Exon20insertion positive – see recommendations above for driver mutation negative NSCLC. In the first-line setting, platinum-based Chemotherapy (ideally with pemetrexed) is recommended. In the second-line setting, amivantamab¹⁹ (CHRYSLIS data) or mobocertinib can be used. Mobocertinib is not Health Canada approved for this indication but at present there is an access programme if Health Canada SAS forms are approved.
- NTRK positive – see recommendations above for driver mutation negative NSCLC. Can use NTRK targeted therapy if accessible, depending on patient comorbidities, age, performance status and patient’s preferences.

Unresectable Stage III NSCLC

- Concurrent chemoradiation with platinum doublet chemotherapy and radical radiation therapy.
- After completion of chemoradiation, monthly consolidation durvalumab for 1 year²⁰ (PACIFIC data).

SCLC: Limited stage

- Four to six cycles of platinum and etoposide chemotherapy with radical radiation therapy. Cisplatin is preferred for limited stage disease, if tolerated.
- After chemoradiation the patient should be considered for prophylactic cranial irradiation or close brain surveillance.

SCLC: Extensive stage

- Chemoimmunotherapy with platinum and etoposide chemotherapy, and immunotherapy. Can use either durvalumab²¹ (CASPIAN data) or atezolizumab²² (IMPOWER 133 data).
- Consider referral to radiation oncology for possible consolidative thoracic irradiation and either prophylactic cranial irradiation or close brain surveillance.
- Continue maintenance durvalumab or atezolizumab until disease progression or poor tolerance.
- Disease recurrence within or beyond 3-6 months can be considered platinum-sensitive and rechallenged with platinum and etoposide.
- Disease recurrence within 3 months is platinum-resistant. Second-line treatment consists of cyclophosphamide, Adriamycin and vincristine (CAV) or topotecan.

Mesothelioma

- First-line treatment options for unresectable malignant pleural mesothelioma include:
 - Ipilimumab/nivolumab (Checkmate 743 data)
 - Carboplatin/pemetrexed (up to 6 cycles)
- Choice of first-line treatment should depend on tumour histology (epithelioid vs sarcomatoid) in addition to patient comorbidities, age, performance status and patient's preferences.
- Second and subsequent line therapy options include retreatment with platinum-pemetrexed, vinorelbine, gemcitabine.

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