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An Endorsement of the ASTRO/ESTRO 2023 Guideline for the Treatment of Patients with Oligometastatic or Oligoprogressive Non-Small Cell Lung Cancer

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This document describes the OH (CCO)-Lung Cancer Disease Site Group endorsement of the 2023 Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline. The original publication is available at https://www.astro.org/patient-care-and-research/clinical-practice-statements/clinical-practice-guidelines/oligometastatic-nsclc.

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For information about the PEBC and the most current version of all reports, please visit the OH (CCO) website at https://www.cancercareontario.ca/en/guidelines-advice or contact the PEBC office at: Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775 E-mail: ccopgi@mcmaster.ca

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An Endorsement of the ASTRO/ESTRO 2023 Guideline for the Treatment of Patients with Oligometastatic or Oligoprogressive Non-Small Cell Lung Cancer

This is a quick reference guide and provides the recommendations only. For the guideline endorsement development process, see the Full Report.

ENDORSEMENT

GUIDELINE OBJECTIVES

The objective of this guideline is to determine the most effective therapies for patients with oligometastatic or oligoprogressive non-small cell lung cancer (NSCLC).

TARGET POPULATION

The target population includes adult patients with oligometastatic or oligoprogressive NSCLC. Several terms were used throughout the American Society for Radiation Oncology/European Society for Radiotherapy & Oncology (ASTRO/ESTRO) 2023 guideline [1] when referencing the oligometastatic disease state: oligorecurrent, oligoprogressive, and oligopersistent. Oligorecurrence refers to the general growth of limited numbers (typically ≤5) of metastatic deposits in patients off systemic therapy. Patients are considered as having oligoprogressive disease if current imaging establishes progression of disease in a limited number (typically ≤5) of existing and/or new sites. For patients with oligometastases receiving active systemic treatment, patients are considered as having oligopersistent disease if current imaging establishes stable disease or partial response of the existing limited disease to therapy. Furthermore, synchronous oligometastatic disease refers to the occurrence of oligometastases de novo at the time of initial diagnosis of NSCLC. Although the presence of a disease-free interval differentiates metachronous from synchronous oligometastatic disease, there is no formal definition of the length of disease-free interval required, with intervals of both three and six months having been used in clinical trials. (ENDORSED WITH MODIFICATION – see below)

INTENDED USERS

The intended users include oncologists and thoracic surgeons involved in the treatment of patients with oligometastatic or oligoprogressive NSCLC.

RECOMMENDATIONS

The Oligometastatic NSCLC Guideline Development Group (GDG) of Ontario Health (Cancer Care Ontario) (OH [CCO]) endorses the recommendations of the ASTRO/ESTRO 2023 guideline, as modified by the endorsement process described in this document [1]. They are reprinted with the permission of ASTRO. A modified version of ASTRO's recommendation grading classification system can be found in Section 2 Table 2.1 [1]. Please see Section 2 Table 2.2 for the original ASTRO/ESTRO 2023 recommendations and any modifications to the recommendations or their scoring system made as well as the reasons for the modifications. Local therapy includes surgical excision, minimally invasive ablation (e.g., radiofrequency ablation), radiation therapy (including conventionally fractionated, stereotactic ablative radiation therapy, stereotactic body radiation therapy (SBRT), and stereotactic radiosurgery), and combinations. Systemic therapy includes targeted therapy, immunotherapy, chemotherapy, and combinations.

Recommendations about patient/disease characteristics for definitive systemic and local therapies (please also see Algorithm 1 on page 5)

1.1. For patients with oligometastatic NSCLC, treatment decisions should be made using a patient-centred multidisciplinary team approach. (strong recommendation, expert opinion) (ENDORSED)

1.2. For patients with oligometastatic NSCLC, if integration of definitive local therapy is indicated, it should only be in the context when it is technically feasible and clinically safe for all disease sites. (strong recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

1.3. For patients with oligometastatic NSCLC, a discussion of definitive local therapy as a component of multimodality treatment approach may be considered irrespective of presence of activating driver mutations. (conditional recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

1.4. For oligometastatic NSCLC, if definitive local therapy is being considered, it is recommended only for patients having up to five distant metastases, diagnosed with appropriate imaging. (strong recommendation, low quality of evidence)
Implementation remark: Despite some prospective trials including patients with up to five extracranial metastases, most patients enrolled had one to two treated oligometastatic lesions, which should be factored into decision-making. (ENDORSED WITH MODIFICATION)

1.5. For patients with synchronous oligometastatic NSCLC, definitive local therapy to all cancer sites in addition to standard-of-care systemic therapy is conditionally recommended. (conditional recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

1.6. For patients with metachronous oligorecurrent NSCLC, definitive local therapy to all oligorecurrent cancer sites in addition to standard-of-care systemic therapy is conditionally recommended. (conditional recommendation, low quality of evidence) (ENDORSED)

1.7. For patients with induced oligopersistent NSCLC, definitive local therapy to all persistent cancer sites in addition to continuing standard-of-care systemic therapy (if well tolerated) is conditionally recommended. (conditional recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

1.8. For patients with induced oligoprogressive NSCLC receiving systemic therapy, definitive local therapy to all progressive cancer sites is conditionally recommended while continuing the current line of systemic therapy. (conditional recommendation, expert opinion) (ENDORSED)

Recommendations about local treatment modality selection criteria for oligometastatic NSCLC 2 (please also see Algorithm 2 on page 6)

2.1. For patients with oligometastatic NSCLC, a patient-centred multidisciplinary discussion of the most appropriate local treatment strategy of radiation therapy (RT) and/or surgery either alone or in combination are recommended. (strong recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

2.2. For patients with oligometastatic NSCLC, RT and/or surgery are recommended as definitive local treatment modalities for the locoregional primary and all oligometastases. (conditional recommendation, low quality of evidence)
Implementation remark: Surgical approach and RT approach will depend on patient factors. (ENDORSED WITH MODIFICATION)

2.3. For patients with oligometastatic NSCLC, highly conformal RT approaches and minimally invasive techniques for surgery are recommended to minimize morbidity. (strong recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

2.4. For patients with oligometastatic NSCLC, deciding between RT and surgery as the definitive local treatment modality should: (strong recommendation, expert opinion)
- Favour RT when multiple organ systems are being treated
- Favour RT when the clinical prioritization is to minimize breaks from systemic therapy (ENDORSED WITH MODIFICATION)

Recommendations about the sequencing and timing of treatment therapies for oligometastatic NSCLC

3.1. For patients with synchronous oligometastatic NSCLC, three or more months of systemic therapy is recommended prior to definitive local therapy. (conditional recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

3.2. For patients with oligometastatic NSCLC, up-front definitive local treatment for *symptomatic* lesions should be prioritized. (strong recommendation, low quality of evidence)
Implementation remark: Symptomatic disease sites (e.g., bone metastases) may also be treated with up-front definitive local therapy. (ENDORSED WITH MODIFICATION)

3.3. For patients with synchronous oligometastatic NSCLC, the temporary pause of systemic therapy during definitive local therapy versus concomitant treatment should be discussed using a multidisciplinary team approach. (strong recommendation, expert opinion) (ENDORSED)

3.4. For patients with synchronous oligometastatic NSCLC, continuation on first-line systemic therapy is conditionally recommended after completion of definitive local therapy. (conditional recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

Recommendations about RT dose-fractionation regimens, planning, and delivery techniques for oligometastatic NSCLC

4.1. For patients with oligometastatic NSCLC, appropriate staging with fluorodeoxyglucose F-18 positron emission tomography (PET)-computed tomography (CT), brain magnetic resonance imaging (MRI), and MRI in cases of suspect or proven spine or liver metastases are recommended. (strong recommendation, high quality of evidence)
Implementation remark: PET-CT scans are not yet approved outside of possibly the PET Access program in Ontario for patients with metastatic NSCLC, but they are recommended for patients with stage IV oligometastatic disease who are being considered for definitive therapy. (ENDORSED WITH MODIFICATION)

4.2. For patients with oligometastatic NSCLC, individual assessment of respiratory motion for targets in the lungs and upper abdomen using four-dimensional CT, fluoroscopy, or MR-cine with appropriate motion compensation is recommended. (strong recommendation, high quality of evidence) (ENDORSED)

4.3. For patients with oligometastatic NSCLC, highly conformal RT using inverse dose planning, appropriate motion management strategies and image-guided RT delivery are recommended. (strong recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

4.4. For patients with oligometastatic NSCLC, a risk-adapted approach using stereotactic RT (preferred), hypofractionated RT, or alternatively definitive chemoradiation based on the location and burden of disease is recommended. (strong recommendation, high quality of evidence) (ENDORSED)

4.5. For patients with oligometastatic NSCLC, definitive local RT should use doses and fractionations which achieve durable local control. (strong recommendation, high quality of evidence)

Implementation remarks:

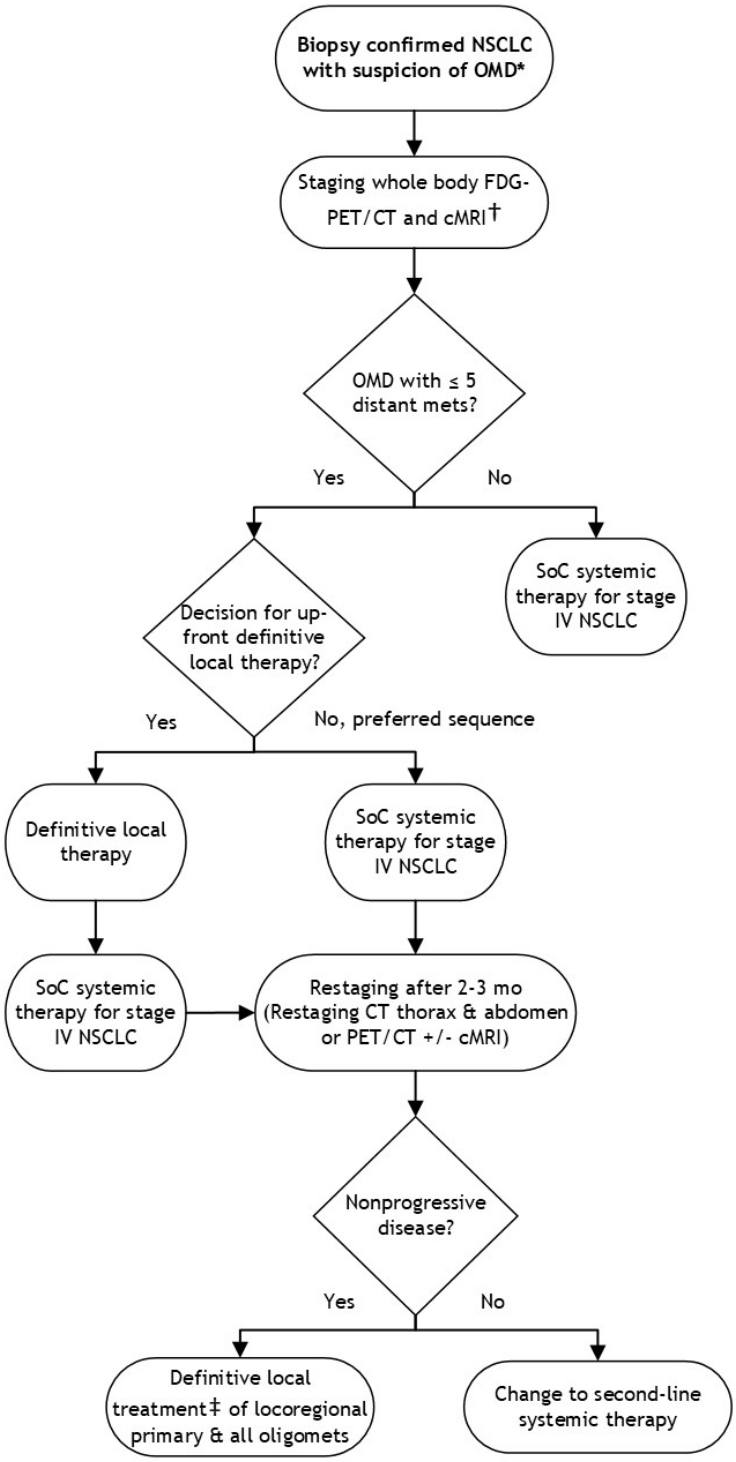
- Durable local control defined as minimum 85% local control at two years.
- Higher biologically effective dose (BED^{10}) (typically >75 Gy) with SBRT alone is associated with optimal local control.
- Lower BED^{10} (50-75 Gy range) is associated with acceptable local control, typically in the setting of combination systemic therapy and SBRT. (ENDORSED)

Recommendations about indications for additional local therapy on disease progression (after definitive local therapy approach)

5.1. In patients previously treated with definitive local therapy for oligometastatic NSCLC who subsequently develop repeat oligoprogression or recurrence, local therapy is conditionally recommended and should be discussed using a multidisciplinary team approach. (conditional recommendation, low quality of evidence) (ENDORSED WITH MODIFICATION)

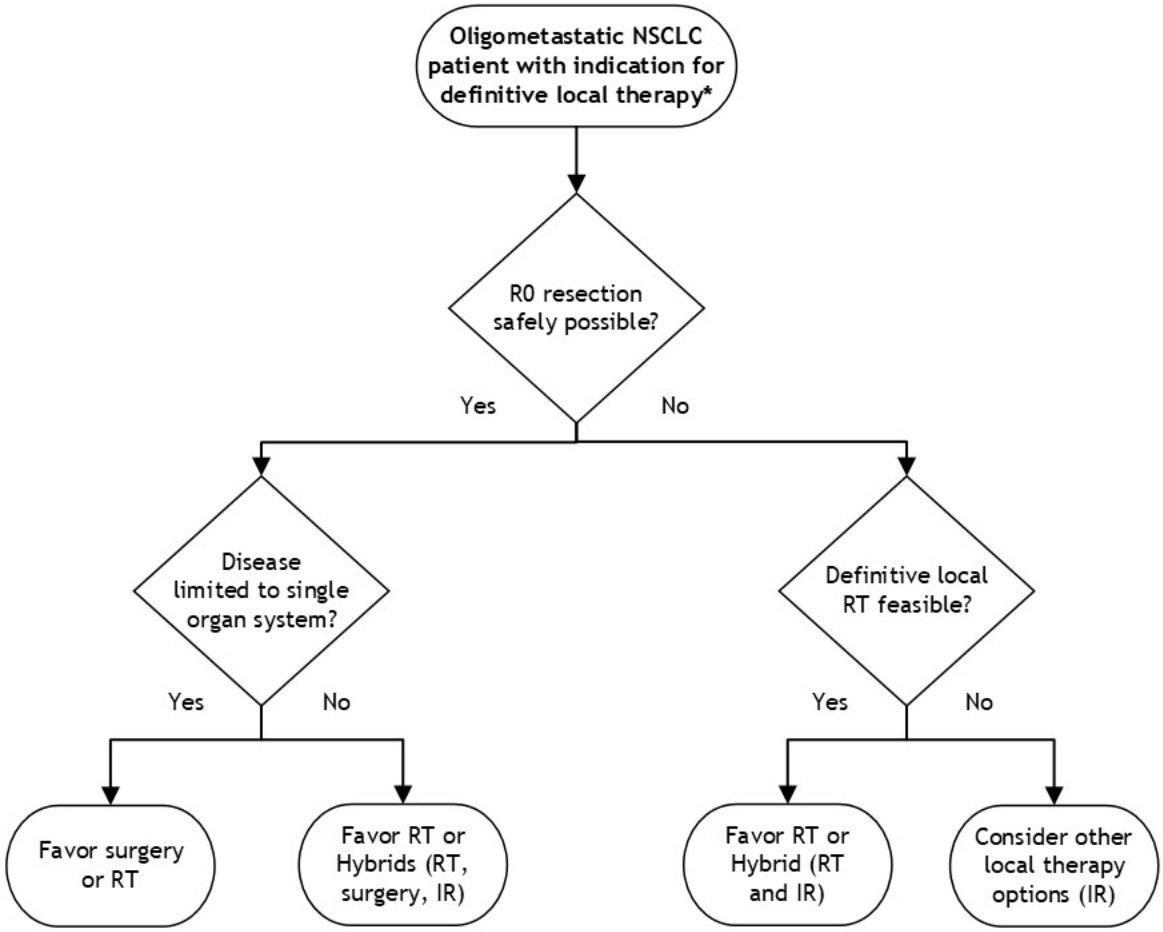
5.2. In patients previously treated with definitive local therapy for oligometastatic NSCLC who subsequently develop repeat oligoprogression or recurrence at sites previously treated with local therapy, re-treatment is conditionally recommended if systemic treatment options are limited, and local therapy can be delivered with toxicity acceptable to the multidisciplinary team and patient. (conditional recommendation, expert opinion) (ENDORSED)

Algorithm 1. Diagnosis and sequencing of local and systemic treatment for synchronous oligometastatic NSCLC. (ENDORSED WITH MODIFICATIONS)



Abbreviations: cMRI = cranial magnetic resonance imaging; CT = computed tomography; FDG PET = fluorodeoxyglucose F-18 positron emission tomography; mets = metastases; MRI = magnetic resonance imaging; NSCLC = non-small cell lung cancer; OMD = oligometastatic disease; SoC = standard of care. *Preferably biopsied OMD as well. †Additional imaging modalities that are reasonable to use in establishing an OMD state include contrast-enhanced chest and upper abdomen CT scan, MRI, bone scan, or PET-MRI. ‡Completion of definitive local treatment of all cancer sites if multimodality treatment was started with local treatment. cMRI†

Algorithm 2. Multidisciplinary decision-making process of definitive RT and surgery for oligometastatic NSCLC. (ENDORSED WITH MODIFICATIONS)



Abbreviations: IR = interventional radiology procedures; NSCLC = non-small cell lung cancer; RT = radiation therapy, which could include stereotactic body radiation therapy, intensity-modulated radiation therapy or radical RT. *Surgical approach and RT approach will depend on patient factors. Adequate tissue sampling should be performed prior to determining resectability.

Reference

1. Iyengar P, All S, Berry MF, Boike TP, Bradfield L, Dingemans AC, et al. Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline. Pract Radiat Oncol. 2023;13(5):393-412.