Therapy for Stage IV Non-Small Cell Lung Cancer Without Driver Alterations

ASCO Living Guideline, Version 2023.3

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Background & Methodology
Introduction

• The treatment of advanced stage IV NSCLC has evolved dramatically in the past decade.

• ASCO launched living practice guidelines for systemic management for patients with stage IV NSCLC with\(^1\) and without driver alterations\(^2\) in 2022, both of which have been updated recently to reflect this rapidly evolving treatment landscape.\(^3-9\)

• The purpose of this guideline is to update the ASCO and Ontario Health (CCO) guidelines on the systemic management of patients with stage IV NSCLC without driver alterations.

• This comprehensive update is a result of possible practice-changing evidence published since the last update by Singh and associates,\(^2\) and subsequent rapid updates published afterwards.\(^3-5\)
ASCO Living Guideline Development Methodology

• The ASCO Evidence Based Medicine Committee (EBMC) living guideline process includes:
  ▪ a ongoing literature review by ASCO guidelines staff
  ▪ an expert panel provides critical review and evidence interpretation to inform guideline recommendations
  ▪ final guideline approval by ASCO EBMC

• The full ASCO Guideline methodology manual can be found at: www.asco.org/guideline-methodology

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Clinical Questions

This clinical practice guideline update addresses two overarching clinical questions:

1. What are the most effective first-line treatment options for patients with stage IV NSCLC without driver alterations, based on cancer subtype?
2. What are the most effective second-line and subsequent treatment options for patients with stage IV NSCLC without driver alterations based on cancer subtype?
Target Population and Audience

Target Population

• Patients with stage IV NSCLC without targetable driver alterations

Target Audience

• Oncology care providers (including primary care physicians, specialists, nurses, social workers, and any other relevant member of a comprehensive multidisciplinary cancer care team), patients, and their caregivers.
Summary of Recommendations
Summary of Recommendations

Note.

• For recommendations with multiple treatment options of the same evidence quality and strength of recommendation, the decision of which agent to offer should be tailored based on discussion of efficacy and toxicity with each patient.

Clinical Question 1

• What are the most effective first-line treatment options for patients with good performance status and the following biomarkers?
Summary of Recommendations

Nonsquamous cell carcinoma, PD-L1 expression
TPS ≥ 50%

1.1. Clinicians should offer single-agent pembrolizumab or cemiplimab or atezolizumab.

1.2. Clinicians may offer pembrolizumab + carboplatin + pemetrexed or cemiplimab + carboplatin + pemetrexed.

1.3. Clinicians may offer atezolizumab + carboplatin + nab-paclitaxel with or without bevacizumab (in the absence of contraindications to bevacizumab).

1.4. Clinicians may offer nivolumab and ipilimumab.
Summary of Recommendations

Nonsquamous cell carcinoma, PD-L1 expression TPS ≥ 50%

1.5. Clinicians may offer nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.

1.6. Clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.
Summary of Recommendations

Nonsquamous cell carcinoma, PD-L1 expression TPS 1%-49%

1.7. Clinicians should offer pembrolizumab + carboplatin + pemetrexed or cemiplimab + carboplatin + pemetrexed.

1.8. Clinicians may offer atezolizumab + carboplatin + (nab)-paclitaxel ± bevacizumab in the absence of contraindications to bevacizumab.

1.9. Clinicians may offer nivolumab and ipilimumab.

2.0. Clinicians may offer nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.
Summary of Recommendations

Nonsquamous cell carcinoma, PD-L1 expression TPS 1%-49%

2.1. Clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.

2.2. For patients who are ineligible for or decline the combination of doublet platinum ± anti-PD-(L)1, clinicians may offer monotherapy with anti-PD-1.
Summary of Recommendations

Nonsquamous cell carcinoma, unknown or negative PD-L1 expression TPS <1%

2.3. Clinicians may offer pembrolizumab + carboplatin + pemetrexed or cemiplimab + carboplatin + pemetrexed.

2.4. Clinicians may offer atezolizumab + carboplatin + (nab)-paclitaxel ± bevacizumab in the absence of contraindications to bevacizumab.

2.5. Clinicians may offer nivolumab and ipilimumab.

2.6. Clinicians may offer nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.
Summary of Recommendations

Nonsquamous cell carcinoma, unknown or negative PD-L1 expression TPS <1%

2.7. Clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.
Summary of Recommendations

**Squamous cell carcinoma, PD-L1 expression TPS ≥ 50%**

3.1. Clinicians should offer single-agent pembrolizumab or cemiplimab or atezolizumab.

3.2. Clinicians may offer pembrolizumab + carboplatin + paclitaxel (or nab-paclitaxel) or cemiplimab + carboplatin + paclitaxel.

3.3. Clinicians may offer nivolumab and ipilimumab.

3.4. Clinicians may offer nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.

3.5. Clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.
Summary of Recommendations

Squamous cell carcinoma, PD-L1 expression TPS 1%-49%

3.6. Clinicians should offer pembrolizumab + carboplatin + paclitaxel (or nab-paclitaxel) or cemiplimab + carboplatin + paclitaxel.

3.7. Clinicians may offer nivolumab and ipilimumab.

3.8. Clinicians may offer nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.

3.9. Clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.

4.0. For patients who are ineligible for or decline the combination of doublet platinum ± anti-PD-(L)1, clinicians may offer single-agent anti-PD-1.
Summary of Recommendations

Squamous cell carcinoma, unknown or negative PD-L1 expression, TPS <1%

4.1. Clinicians should offer pembrolizumab + carboplatin + paclitaxel (or nab-paclitaxel) or cemiplimab + carboplatin + paclitaxel.

4.2. Clinicians may offer nivolumab and ipilimumab.

4.3. Clinicians may offer nivolumab and ipilimumab plus two cycles of platinum-based chemotherapy.

4.4. Clinicians may offer durvalumab and tremelimumab plus platinum-based chemotherapy.
Summary of Recommendations

Patients with unspecified histology

4.5. Patients with advanced lung cancer should be referred to interdisciplinary palliative care teams (consultation) that provide inpatient and outpatient care early in the course of disease, alongside active treatment of their cancer.

4.6. For patients who are not candidates for immune checkpoint inhibitor therapy, clinicians should offer platinum doublet combination therapy for patients with preserved PS.

4.7. Clinicians may offer nonplatinum therapy combinations for patients who have contraindications to platinum therapy.
Summary of Recommendations

Patients with contraindications to bevacizumab

4.8. Bevacizumab should be avoided for patients with squamous cell carcinoma histologic type, clinically significant hemoptysis, inadequate organ function, ECOG PS > 1, clinically significant cardiovascular disease, or medically uncontrolled hypertension.

4.9. Maintenance bevacizumab given with pemetrexed has no survival advantage and significant increased toxicity compared to maintenance pemetrexed or bevacizumab alone.
Summary of Recommendations

Clinical Question 2

• What are the most effective second-line and subsequent treatment options for patients with good performance status?

Patients previously treated with immune checkpoint therapy without chemotherapy

5.0. Clinicians should offer platinum doublet chemotherapy.

Informal consensus

Evidence Quality

Low

Strength of Recommendation

Strong
Summary of Recommendations

Patients previously treated with chemotherapy and immune checkpoint therapy

5.1. Clinicians should offer docetaxel with or without ramucirumab if the patient has already received platinum-based chemotherapy.

5.2. Clinicians may offer pemetrexed or gemcitabine if the patient has already received platinum-based chemotherapy.
Discussion
Patient and Clinician Communication

• With the advent of new targeted therapies that result in survival gains, patient and clinician communication remains a cornerstone of optimal cancer care.

• As previously described in the 2021 guideline,\textsuperscript{10} clinicians should be facile in core communications skills that apply across the continuum of health care.

• In particular, when discussing treatment options, clinicians should provide information about the benefits and burdens of any treatment and check the patient’s understanding of these benefits and burdens.

• It is important to foster shared decision making when there are multiple therapeutic options.\textsuperscript{11}
Cost Implications

• Patient out-of-pocket costs are a barrier to initiating and adhering to recommended cancer treatments.\textsuperscript{12,13}

• The prior guideline reviews the complexities of varied out-of-pocket costs due to insurance coverage, noting how cost considerations are a part of shared decision-making.

• Financial toxicity assessment should be routinely undertaken, and financial challenges in accessing cancer care should be an issue for discussion between clinicians and patients.\textsuperscript{10}
Additional Resources

• More information, including a supplement and clinical tools and resources, is available at www.asco.org/living-guidelines

• Patient information is available at www.cancer.net
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Abbreviations

- ASCO, American Society of Clinical Oncology
- CCO, Cancer Care Ontario
- EBMC, Evidence Based Medicine Committee
- ECOG, Eastern Cooperative Oncology Group
- nab, nanoparticle albumin-bound
- NSCLC, non-small cell lung cancer
- PD-L1, programmed death ligand 1
- PS, performance status
- TPS, tumor proportion score

References
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