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# Management of Stage III NSCLC

## ASCO Guideline Rapid Recommendation Update

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Singh & Daly et al.

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# Background & Methodology

# Introduction

- In 2021, ASCO published a guideline on the management of stage III NSCLC.<sup>1</sup>
- Three RCTs were published in 2022<sup>2</sup> and 2023<sup>3,4</sup> and prompted this amendment to the 2021 guideline.

# Development Methodology

- A targeted electronic literature search to identify RCTs in this patient population was conducted and three relevant studies were found.
- Members from the original Expert Panel reconvened to assess key evidence from the CheckMate 816,<sup>2</sup> ADAURA,<sup>3,4</sup> and KEYNOTE-671<sup>5</sup> trials and to create and approve the revision to the recommendations.
- The ASCO Guideline methodology manual can be found at: [www.asco.org/guideline-methodology](http://www.asco.org/guideline-methodology)

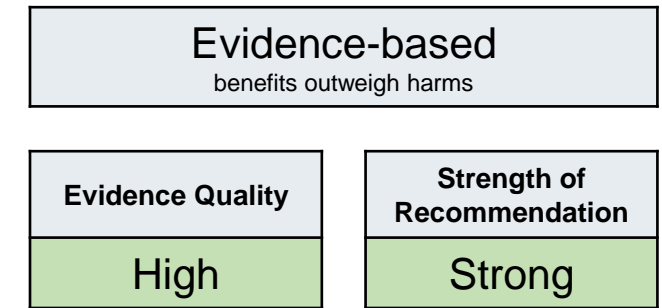
# 2

## Rapid Recommendation Update

# Rapid Recommendation Update

## Recommendation 3.2

- Patients with stage III NSCLC who are planned for surgical resection should receive neoadjuvant chemoimmunotherapy, neoadjuvant chemotherapy, or neoadjuvant concurrent chemoradiation.



# Rapid Recommendation Update

## Recommendation 4.2

- Patients with resected stage III NSCLC with *EGFR* exon 19 deletion or exon 21 L858R mutation should be offered adjuvant osimertinib after platinum-based chemotherapy.

Evidence-based benefits outweigh harms	
Evidence Quality	Strength of Recommendation
High	Strong



# 3

## Summary of Previous Recommendations

# Summary of Previous Recommendations

- Recommendations that are unchanged are provided in the following slides

# Summary of Previous Recommendations

## Clinical Question 1

- What is the appropriate evaluation and staging work up for patients with suspected stage III NSCLC?

## Recommendation 1.1

- For patients with suspected stage III NSCLC, an evaluation to exclude metastatic disease should include, at a minimum: history and physical exam and CT scan of chest and upper abdomen (with contrast, unless contraindicated).

Informal consensus benefit outweighs harm	
Evidence Quality	Strength of Recommendation
Low	Strong

***Clinical interpretation:*** Any suspected metastatic site identified on CT should be confirmed pathologically with biopsy. In general, biopsy sites should be selected to confirm highest possible disease stage, and to maximize tissue yield.

# Summary of Previous Recommendations

## Recommendation 1.2

- Following evaluation with CT scan as per Recommendation 1.1, FDG PET with CT scan and brain imaging should be performed.

Evidence-based  
benefit outweighs harm

Evidence Quality  
High

Strength of Recommendation  
Strong

## Recommendation 1.3

- For patients with suspected stage III NSCLC, who are candidates for curative-intent treatment, mediastinal lymph node status should be confirmed by pathologic assessment.

Evidence-based  
benefit outweighs harm

Evidence Quality  
Moderate

Strength of Recommendation  
Strong

# Summary of Previous Recommendations

## Recommendation 1.4

- For patients who require pathologic assessment of lymph node status, endoscopic techniques should be offered as the initial staging modality.

Evidence-based  
benefit outweighs harm

Evidence Quality  
Moderate

Strength of Recommendation  
Strong

## Recommendation 1.5

- For patients who require pathologic assessment of lymph node status but for whom endoscopic staging is either unavailable or inconclusive, surgical confirmation of mediastinal stage should be performed.

Evidence-based  
benefit outweighs harm

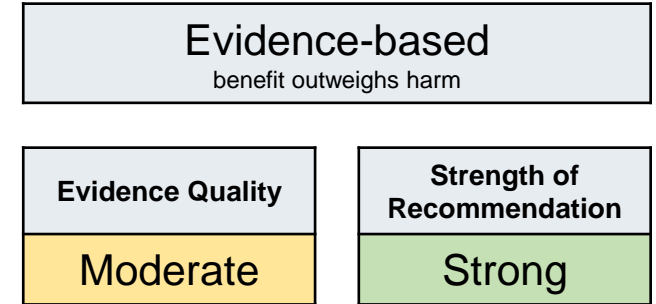
Evidence Quality  
Moderate

Strength of Recommendation  
Strong

# Summary of Previous Recommendations

## Recommendation 1.6

- For patients who have suspected or confirmed stage III NSCLC, multidisciplinary discussion should occur prior to the initiation of any treatment plan.



## Good Practice Point

- Biopsy should generally be performed from the site that would establish the highest stage when feasible. Potential tissue yield for pathologic analysis and molecular sequencing should also be considered.

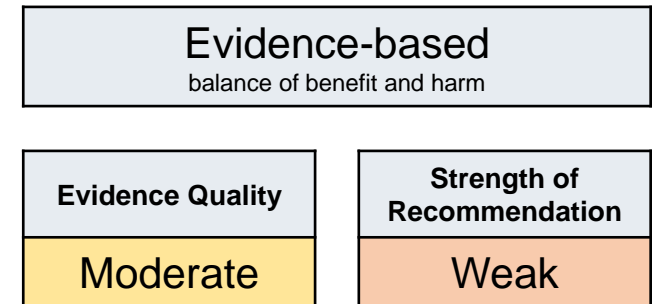
# Summary of Previous Recommendations

## Clinical Question 2

- Which patients with stage III NSCLC may be considered for surgical resection?

### Recommendation 2.1

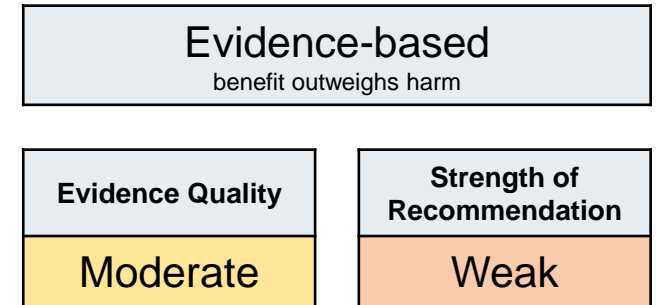
- For patients with stage IIIA (N2) NSCLC, induction therapy followed by surgery (with or without adjuvant therapy) may be offered if all of the following conditions are met:
  - a) A complete resection (R0) of the primary tumor and involved lymph nodes is deemed possible;
  - b) N3 lymph nodes are deemed to be not involved by multidisciplinary consensus
  - c) Perioperative (90-day) mortality is expected to be low ( $\leq 5\%$ ).



# Summary of Previous Recommendations

## Recommendation 2.2

- For selected patients with T4N0 disease (by size or extension), surgical resection may be offered if medically and surgically feasible following multidisciplinary review.



## Good Practice Points

- Patients with stage III NSCLC generally should not be excluded from consideration for surgery by nonsurgical physicians.
- Presence of oncogenic driver alterations, available therapies, and patient characteristics should be taken into account.
- Patients and providers should consider enrollment on clinical trials when appropriate.



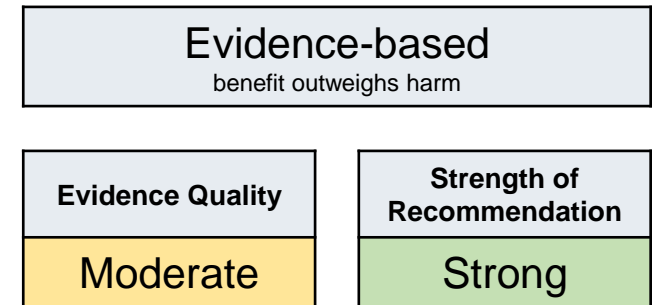
# Summary of Previous Recommendations

## Clinical Question 3

- Which patients with potentially resectable stage III NSCLC should be considered for neoadjuvant therapy?

## Recommendation 3.1

- Patients who are planned for a multimodality approach incorporating surgery as defined in Recommendation 2.1 should receive systemic neoadjuvant therapy.



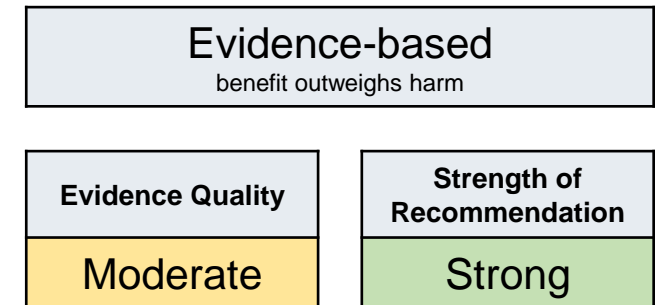
# Summary of Previous Recommendations

## Recommendation 3.2

- See updated recommendation

## Recommendation 3.3

- For patients with resectable superior sulcus disease, neoadjuvant concurrent chemoradiation should be administered.



# Summary of Previous Recommendations

## Clinical Question 4

- Which patients with resected stage III NSCLC should be considered for adjuvant therapy?

### Recommendation 4.1

- Patients with resected stage III NSCLC who did not receive neoadjuvant systemic therapy should be offered adjuvant platinum-based chemotherapy.

Evidence-based benefit outweighs harm	
Evidence Quality	Strength of Recommendation
High	Strong

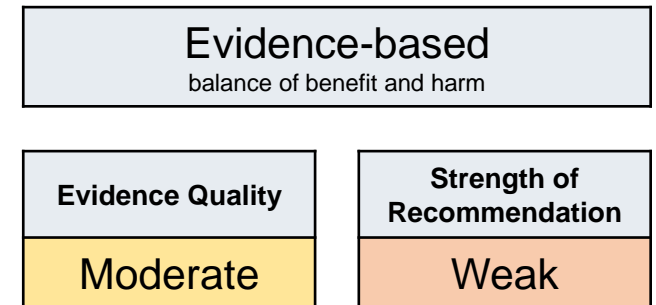
# Summary of Previous Recommendations

## Recommendation 4.2

- See updated recommendation.

## Recommendation 4.3

- For patients with completely resected NSCLC with mediastinal N2 involvement without extracapsular extension who have received neoadjuvant or adjuvant platinum-based chemotherapy, postoperative radiation therapy should not be routinely offered.



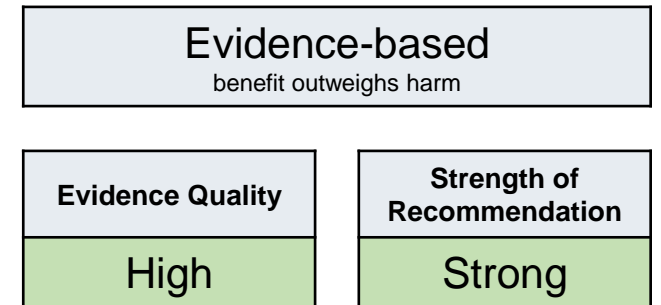
# Summary of Previous Recommendations

## Clinical Question 5

- What is the appropriate management for patients with unresectable stage III NSCLC?

### Recommendation 5.1

- Patients with stage III NSCLC who are medically or surgically inoperable and with good performance status should be offered concurrent instead of sequential chemotherapy and radiation therapy.



# Summary of Previous Recommendations

## Recommendation 5.2

- Concurrent chemotherapy delivered with radiation therapy for definitive treatment of stage III NSCLC should include a platinum-based doublet, preferably cisplatin plus etoposide, carboplatin plus paclitaxel, cisplatin plus pemetrexed (non-squamous only), or cisplatin plus vinorelbine.

**Qualifying statement:** *Carboplatin may be substituted for cisplatin in patients with contraindications to or deemed ineligible for cisplatin.*

Evidence-based benefit outweighs harm	
Evidence Quality	Strength of Recommendation
High	Strong

# Summary of Previous Recommendations

## Recommendation 5.3

- Patients with stage III NSCLC who are not candidates for concurrent chemoradiation but are candidates for chemotherapy should be offered sequential chemotherapy and radiation therapy over radiation alone.

Evidence-based  
benefit outweighs harm

Evidence Quality  
High

Strength of Recommendation  
Strong

## Recommendation 5.4

- Patients with stage III NSCLC receiving concurrent chemoradiation should be treated to 60 Gy.

Evidence-based  
balance of benefit and harm

Evidence Quality  
High

Strength of Recommendation  
Strong

# Summary of Previous Recommendations

## Recommendation 5.5

- Doses higher than 60 Gy and up to 70 Gy may be considered for selected patients, with careful attention to doses to heart, lungs, and esophagus.

Evidence-based  
benefit outweighs harm

Evidence Quality  
Low

Strength of Recommendation  
Strong

## Recommendation 5.6

- Patients with stage III NSCLC receiving definitive radiation without chemotherapy in standard fractionation may be considered for radiation dose escalation and for modest hypofractionation from 2.15-4 Gy per fraction.

Evidence-based  
balance of benefit and harm

Evidence Quality  
Low

Strength of Recommendation  
Weak



# Summary of Previous Recommendations

## Recommendation 5.7

- Patients with stage III NSCLC receiving concurrent chemoradiation without disease progression during the initial therapy should be offered consolidation durvalumab for up to 12 months.

**Qualifying statement:** *There is insufficient evidence to alter the recommendation for consolidation durvalumab following concurrent chemo-radiation for molecularly defined subgroups (namely patients with an oncogenic driver alteration or those with low or no expression of PD-L1).*

Evidence-based benefit outweighs harm	
Evidence Quality	Strength of Recommendation
High	Strong

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## Additional Information

# Additional Resources

- More information, including clinical tools and resources, is available at [www.asco.org/thoracic-cancer-guidelines](http://www.asco.org/thoracic-cancer-guidelines)
- Patient information is available at [www.cancer.net](http://www.cancer.net)

# Guideline Panel Members

Name	Affiliation/Institution	Role/Area of Expertise
Megan Daly, MD (co-chair)	University of California, Davis, CA	Radiation Oncology
Navneet Singh, MD (co-chair)	Postgraduate Institute of Medical Education & Research, Chandigarh, India	Medical Oncology
Mara Antonoff, MD	MD Anderson Cancer Center, Houston, TX	Surgical Oncology
Douglas A. Arenberg, MD	University of Michigan, Ann Arbor, MI	Pulmonology; ACCP Representative
Jeffrey Bradley, MD	Emory University, Atlanta, GA	Radiation Oncology; ASTRO Representative
Elizabeth David, MD	University of Southern California, Los Angeles, CA	Surgical Oncology
Frank Detterbeck, MD	Yale Cancer Center, New Haven, CT	Surgical Oncology; ACCP Representative
Martin Früh, MD, PhD	Department of Medical Oncology/ Hematology, Cantonal Hospital of St. Gallen, St. Gallen, Switzerland; University of Bern, Bern, Switzerland	Medical Oncology
Matthew Gubens, MD, MS	University of California San Francisco, CA	Medical Oncology
Amy Moore, PhD	LUNGeity Foundation, Chicago, IL	Patient Representative
Sukhmani K. Padda, MD	Department of Medicine, Division of Oncology, Cedars-Sinai Medical Center, Los Angeles, CA	Medical Oncology
Jyoti D. Patel, MD	Northwestern University-Feinberg School of Medicine, Chicago, IL	Medical Oncology
Tanyanika Phillips, MD, MPH	City of Hope, Lancaster, CA	Community Oncology
Angel Qin, MD	University of Michigan, Ann Arbor, MI	Medical Oncology
Clifford Robinson, MD	Washington University, St. Louis, MO	Radiation Oncology
Charles B. Simone, II, MD	New York Proton Center and Memorial Sloan Kettering Cancer Center, New York, NY	Radiation Oncology
Nofisat Ismaila, MD, MSc	American Society of Clinical Oncology, Alexandria, VA	ASCO Practice Guideline Staff (Health Research Methods)

# Abbreviations

- ASCO, American Society of Clinical Oncology
- CT, computed tomography
- EBMC, Evidence Based Medicine Committee
- *EGFR*, epidermal growth factor receptor
- FDG, fluorodeoxyglucose
- NSCLC, non–small-cell lung cancer
- PD-L1, programmed death ligand 1
- PET, positron emission tomography
- RCTs, randomized controlled trials

# References

1. Daly ME, Singh N, Ismaila N, et al: Management of Stage III Non-Small-Cell Lung Cancer: ASCO Guideline. J Clin Oncol 40:1356-1384, 2022
2. Forde PM, Spicer J, Lu S, et al: Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. N Engl J Med 386:1973-1985, 2022
3. Herbst RS, Wu YL, John T, et al: Adjuvant Osimertinib for Resected EGFR-Mutated Stage IB-III A Non-Small-Cell Lung Cancer: Updated Results From the Phase III Randomized ADAURA Trial. J Clin Oncol 41:1830-1840, 2023
4. Herbst RS, Tsuboi M, John T, et al: Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–III A non-small cell lung cancer (NSCLC). ASCO Annual Meeting 2023. LBA3 ABSTRACT #401500.
5. Wakelee H, Liberman M, Kato T, et al: Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer. N Engl J Med, 2023

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