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Management of Stage III NSCLC

ASCO Guideline Rapid Recommendation Update

Singh & Daly et al.

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1 Background & Methodology

Introduction

- In 2021, ASCO published a guideline on the management of stage III NSCLC.[1]
- Three RCTs were published in 2022[2] and 2023[3,4] 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,[2] ADAURA,[3,4] and KEYNOTE-671[5] 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

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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.

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

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

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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	**Strength of Recommendation**
High	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	**Strength of Recommendation**
Moderate	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	**Strength of Recommendation**
Moderate	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	**Strength of Recommendation**
Moderate	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.

Evidence-based benefit outweighs harm	
Evidence Quality	**Strength of Recommendation**
Moderate	Strong

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 (≤ 5%).

Evidence-based balance of benefit and harm	
Evidence Quality	**Strength of Recommendation**
Moderate	Weak

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.

Evidence-based benefit outweighs harm	
Evidence Quality	**Strength of Recommendation**
Moderate	Weak

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.

Evidence-based benefit outweighs harm	
Evidence Quality	**Strength of Recommendation**
Moderate	Strong

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.

Evidence-based benefit outweighs harm	
Evidence Quality	**Strength of Recommendation**
Moderate	Strong

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.

Evidence-based balance of benefit and harm	
Evidence Quality	**Strength of Recommendation**
Moderate	Weak

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.

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

Summary of Previous Recommendations

Recommendation 5.2

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

- 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.*

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	**Strength of Recommendation**
High	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	**Strength of Recommendation**
High	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	**Strength of Recommendation**
Low	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	**Strength of Recommendation**
Low	Weak

Summary of Previous Recommendations

Recommendation 5.7

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

- 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).*

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4 Additional Information

Additional Resources

- More information, including clinical tools and resources, is available at www.asco.org/thoracic-cancer-guidelines

- Patient information is available at www.cancer.net

Guideline Panel Members

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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

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