



TREATMENT & MANAGEMENT OF UNRESECTABLE STAGE III NSCLC

A Radiation Oncologist's Checklist

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I am a community-based radiation oncologist focused on treating patients with unresectable Stage III non-small cell lung cancer (NSCLC). As a member of a multidisciplinary team (MDT), I feel that treating NSCLC is truly a collaborative effort and believe that having all parties participate in the patient's journey can only improve the diagnosis, treatment, and management of side effects.

When transitioning to private practice, I noticed that while there was communication between providers, oftentimes the urgency for next steps was not present. I found having a checklist helped ensure that my patients were being taken care of appropriately. After speaking to numerous other providers, I came to the conclusion that this checklist may be helpful for other community radiation oncologists and engage their staff in the process.

I am hopeful that this checklist will complement and reinforce processes already occurring in clinics to ensure that patients have access to the best available care. In a time where providers have electronic medical records to manage, staff to oversee, and clinics to run, I believe that this checklist may help ensure that nothing is missed when it comes to treating patients with unresectable Stage III NSCLC.

*Recommendations and approaches may vary among patients

Treatment & Management of Unresectable Stage III NSCLC

A Radiation Oncologist's Checklist

Checklist

1. Referral

- Receive referral from primary care physician (PCP)/pulmonologist/medical oncologist^{1,2}
- Simultaneous referral to medical oncology and radiation oncology will decrease time to treatment¹⁻³

2. Staging

- Confirm that all staging is complete before proceeding with the treatment plan⁴⁻⁵
- Positron emission tomography (PET)/magnetic resonance imaging (MRI)^{4,6}
- Endobronchial ultrasound (EBUS) performed on questionable lymph nodes⁶
- If not previously performed, coordinate with the medical oncologist to have a prescriptive plan around the sequence of events to confirm a patient's clinical stage through PET (if not previously performed) while developing a radiation plan*

3. Multidisciplinary discussion and treatment recommendation¹

- Align with multidisciplinary team (MDT) on treatment plan (tumor board or phone call)¹
- Phone call between the radiation oncologist and the medical oncologist to ensure agreement and plan before providing treatment recommendation to the patient*
 - Align with medical oncologist on ordering a follow-up scan during concurrent chemoradiation therapy (CRT) for immediately after completion of radiotherapy. *Dr Whitley orders post-CRT scan during the fourth week of CRT
- Communicate with the medical oncologist to build a protocol for up-front prior authorization of immunotherapy to be used post cCRT in eligible patients*

4. Initial discussion with patient and family regarding overall plans of care¹

- Reinforce curative intent in unresectable Stage III setting*
- Concurrent CRT followed by immunotherapy (pending interval evaluation)⁷

5. Development of a radiation treatment plan⁸

- PET/computed tomography (CT) fusion plan⁹
- Evaluate intensity-modulated radiotherapy (IMRT) vs 3D conformal radiotherapy (RT)¹⁰
- Confirm radiation dose^{4,11}
- Dose-volume histogram (DVH) for^{12,13}:
 - Lung constraints
 - Heart constraints
 - Esophagus constraints

6. Dose

- 60 Gy (RTOG 0617) to 66 Gy, if meeting dose tolerances^{4,14,15}

*General guidance gathered from discussions with a physician based on his opinion and experience.

7. Radiation oncologist's discussion with medical oncologist/nurse practitioner (NP)

- Discuss side effect expectations based on treatment plan¹⁶
- Manage expectations – early and rapid evaluation and treatment management¹⁶
 - General adverse event (AE) management protocol
 - Esophagitis management plan¹⁶⁻¹⁸
 - Pneumonitis management plan¹⁶
- Education targeting radiation oncology nurses and radiation therapy technologists (RTTs) to help in early identification of side effects¹⁶
- Discuss concurrent systemic therapy and chemotherapy-related adverse events¹
- Reinforce the overall treatment plan with the patient, including expected adverse events and their management^{1,8}

8. Scans and follow-up appointments*

- Communicate the number of radiation treatments and expected end date of radiation therapy to the medical oncologist*
 - While the patient is undergoing CRT, schedule post-CRT scans to occur after CRT completion. *Dr Whitley orders post-CRT scans during the fourth week of CRT to occur 1-2 days after CRT completion
 - Confirm with medical oncology NP once post-CRT scan is ordered*
 - Approximately 2 weeks before the completion of concurrent CRT, schedule follow-up appointment with the medical oncologist for approximately 1 week after CRT completion (phone call recommended)*
 - Actively manage toxicities in coordination with the medical oncologist to allow timely initiation of immunotherapy, pending scans^{1,18}

9. Radiation oncology follow-up¹⁹

- Follow-up appointment with the patient 2 weeks post-CRT completion*
 - Confirm that the patient has seen the medical oncologist and is scheduled to go on immunotherapy treatment, if applicable*
 - Continue to manage AEs to help allow for timely immunotherapy initiation^{1,18}
- Follow up for 5 years or longer following concurrent CRT*

General Tips for Private Practice/ Community-Setting Radiation Oncologists

- Early, rapid communication is vital for treating and managing unresectable Stage III NSCLC patients. Communication through phone calls or text messages works best*
- Obtain referrals from both the PCP and the pulmonologist. This should be done at the same time when the patient is referred to the medical oncologist¹⁻³
- Discussion with MDT members is critical to treatment success^{4,16,20}
- Limit assumptions of a patient's tolerability to other specialties' therapy (chemotherapy vs RT) without discussion*

*General guidance gathered from discussions with a physician based on his opinion and experience.

This checklist was created based on the physician's experience and does not represent the views or opinions of AstraZeneca.

1. Patient referral to specialists

- ❑ Simultaneous referral to medical oncology and radiation oncology will decrease time to treatment^{1,3}

TIPS

1. Work with the medical oncologist to meet with referring pulmonologists and primary care providers to create a process in which all patients with Stage III NSCLC are referred to both specialties (medical and radiation oncologists) simultaneously. This will allow the radiation oncologist to evaluate the patient and create a treatment plan while the medical oncologist is completing the staging assessment.*
2. Attendance at pulmonary nodule clinics and screening center meeting may be a place to build processes with referring pulmonologists and primary care providers.*

2. Accurate staging is essential

- ❑ If not previously performed, coordinate with the medical oncologist to have a prescriptive plan around the sequence of events to confirm a patient's clinical stage through PET (if not previously performed) while developing a radiation plan^{1,4}

TIP*

1. PET scan reports *can be available as soon as 2 hours* after the scan. Gain agreement from the medical oncologist to see patients within 1-2 days from the PET scan. The radiation oncologist can use this time to create the radiation plan, which typically takes 1 week. Holding each other accountable may push each to complete the process more quickly.
- ❑ Confirm that all procedures needed for staging are completed before proceeding with the treatment plan^{4,5}
 - ❑ PET/MRI scans performed to confirm unresectable Stage III NSCLC^{4,6}
 - ❑ EBUS performed on questionable lymph nodes⁶

3. Discussion with MDT on treatment recommendation and care

- ❑ Align with MDT on treatment plan¹

TIP

1. Tumor board meetings are recommended to have this discussion. If that is not feasible, a live meeting or phone conversation between the medical oncologist and the radiation oncologist is strongly recommended¹
- ❑ Communicate with the medical oncologist to build a protocol for up-front prior authorization of immunotherapy to be used post cCRT in eligible patients*
 - ❑ Phone call to ensure agreement between different HCPs on the multidisciplinary team; discussion with patient on recommendation¹
 - ❑ Align with medical oncologist on ordering a follow-up scan during CRT for immediately after completion of radiotherapy. *Dr Whitley orders post-CRT scan during the fourth week of CRT
 - a. This may help reduce delays due to prior authorization or scheduling requirements

4. Initial discussion with patients and family members regarding overall plans of care¹

- ❑ Reinforce curative intent in unresectable Stage III setting with patients, caregivers, and family members*
- ❑ Remind patients, caregivers, and family members of the long-term treatment plan: combined modality CRT followed by immunotherapy (pending interval evaluation)⁷

TIP*

1. Radiation oncologist should reinforce the steps of the entire treatment plan frequently during CRT. Patients will likely be interested in whether the treatment is working, and while providing updates on the accuracy of the plan and AE management, it is an opportunity to reinforce the overall plan and next steps.

5. Development of a radiation treatment plan

- ❑ PET/CT fusion scan should be performed. PET/CT fusion scanning provides a higher sensitivity and specificity over CT alone.⁹ The impact of using PET/CT fusion has changed decisions on whether a patient should be treated with curative intent, prescribed radiation dose, and volume to treat*
 1. Avoid treating post-obstruction lung consolidation. PET/CT may be useful in delineating tumor vs postobstruction consolidation.
- ❑ Comparison of radiation techniques: IMRT vs 3D conformal RT¹⁴
 - i. IMRT: On the basis of a secondary analysis of the RTOG 0617 phase III randomized clinical trial, IMRT provides lower dose volumes to critical organs (lung, heart, esophagus). This technique also lowers the risk of patients developing higher-grade pneumonitis¹⁴
 - ii. 3D conformal RT should be used for specific cases*
 1. Patients with left upper lobe with adjacent prevascular (level 5/6 lymph nodes) involvement may possibly benefit from treatment with 3D conformal RT*
 2. Other select cases*:
Notes: 3D conformal RT may have a better lung dosimetry plan than does IMRT
 - a. 3D conformal RT may provide equivalent coverage and lower organ doses because IMRT can spill additional low-dose radiation
 - iii. Avoid running the lung dosimetry plan for both 3D conformal RT and IMRT if you know that you will have a better plan with IMRT. However, if not sure which plan is better, or if insurance requires, run both
 - iv. IMRT is the default, while insurance may think 3D conformal RT is the default
- ❑ Dose-volume histogram and organs of risk
 - ii. Lung constraints: Below are recommended criteria for constraints based on previous studies*:
 1. V20 Gy: In the RTOG 0617 phase III randomized clinical trial, V20 Gy lung constraints revealed less than 37% of the total.^{21,22}
 - a. The following are measures to try to reduce V20 to the lungs before starting to decrease the treatment dose:
 - i. In the RTOG 0617 study, the clinical target volume (CTV) had a margin of 1 cm, but CTV was allowed to drop to 5 mm²¹
 - ii. Ensure that respiratory gating (ie, motion management) is utilized to minimize the margin of converting CTV to planning treatment volume (PTV)²¹
 2. Mean lung dose: In the RTOG 1308 study, dosimetric compliance criteria for mean lung dose was less than 20 Gy²³
 3. V5 Gy: In the RTOG 1308 study, dosimetric compliance criteria for V5 Gy was 60% or less²³
 - ii. Heart constraints²³: Below are recommended criteria for constraints based on previous studies*:
 1. V30 Gy: In the RTOG 1308 study, dosimetric compliance criteria for V30 Gy should be 50% or less

2. V45 Gy: In the RTOG 1308 study, dosimetric compliance criteria for V45 Gy should be 35% or less
3. Maximum dose (D_{max}) 0.03 cc: Dosimetric compliance criteria for D_{max} should be 0.03 cc <70 Gy based on the RTOG 1308 study.²³ The RTOG 0617 study examined a higher dose of 74 Gy, which is believed to fail due to higher dose to the heart²¹

*Note: The radiation oncologist and the dosimetrist could also look at the CTV margin and convert CTV to PTV to decrease the risk of treatment dose to the heart**

iii. Esophageal constraints

1. Mean dose: On the basis of the RTOG 0617 study, dosimetric criteria should be less than 34 Gy.²¹
2. 74 Gy: On the basis of the RTOG 1308 study, dosimetric criteria should be less than or equal to 1 cc of the partial circumference²³
3. V50 Gy should be less than 40% since a higher percentage may increase the risk of esophagitis¹⁶
4. D_{max} less than 105%: When maximum dose is outside of PTV <58 Gy, esophageal stricture may occur.^{*24} Avoid high doses to small areas of the esophagus

6. Radiation dose

- The recommended dose for radiotherapy for patients with unresectable Stage III NSCLC is 60 Gy to 66 Gy⁴

Notes:

- 60 Gy is the dose that should be used, but there are data showing benefit at 66 Gy if all of the constraints are met; data from the RTOG 0617 study show that 74 Gy is harmful^{16,21,25}
- If the dosimetrist has exhausted the possibility to meet constraints, the treatment dose should be decreased to 58 Gy and/or lower to 44 Gy, and re-simulate*

7. Discussions between the radiation oncologist and the medical oncologist/NP

- On the basis of the treatment plan, discuss with colleagues and other members of the MDT about the expected side effects that may occur²⁶
- Expected management of side effects: side effects should be managed proactively with early detection and rapid management¹⁶
- Esophagitis
 - The grade of esophagitis should be figured out as soon as possible, and it is likely that the patient will notice the effects first. Patients should communicate any AEs to the radiation oncology nurse as soon as possible. The radiation oncologist should pre-treat patients if there are any concerns*

- Managing esophagitis can include oral sucralfate, Neurontin® (gabapentin) for pain management, stomatitis cocktail, “magic” or “miracle” mouthwash, and antacid medications¹⁶⁻¹⁸
- Prophylactic or early intervention should be conducted to decrease the duration of esophagitis*

Pneumonitis

- The grade of pneumonitis should be determined as soon as possible.¹⁶ There should be a mutual discussion with medical oncology to develop a management plan*
- Management plans for pneumonitis can include steroids¹⁶ and radiation dose adjustments*
- If pneumonitis develops while on immunotherapy, discuss prescribing the patient an appropriate high dose of steroids*

Chemotherapy-related AEs²⁶

- Avenue for phone discussion

Education of radiation oncology nurses and RTTs for early identification of side effects¹⁶

Discuss with the MDT the patient’s concurrent systemic therapy and chemotherapy-related adverse events¹

Ensure reinforcement of the overall treatment plan with the patient, including expected adverse events and their management⁸

8. Scans and follow-up appointments*

- Communicate the number of radiation treatments and expected end date of radiation therapy*
 - In the fourth week of concurrent CRT, schedule follow-up scans 1-2 days after CRT completion*
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9. Radiation oncologist follow-up

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- Follow up for 5 years or longer following concurrent CRT*

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