

Dr. Alex Whitley

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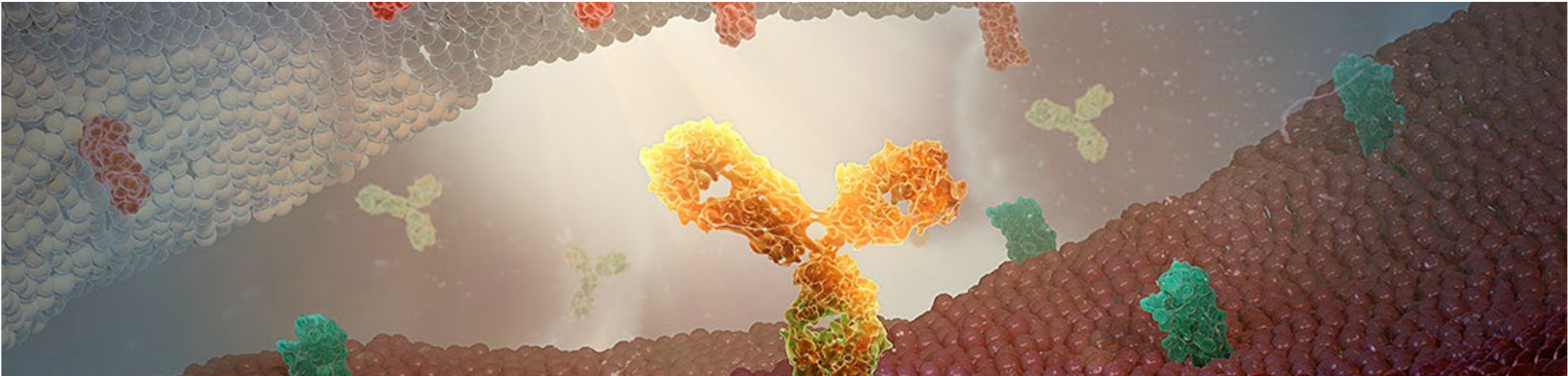
Dr. Mohammad Jafri

DeTar Cancer Center, Victoria, TX



Roundtable Discussion:

Working Together to Advance Guideline-Recommended Care for Early-Stage NSCLC



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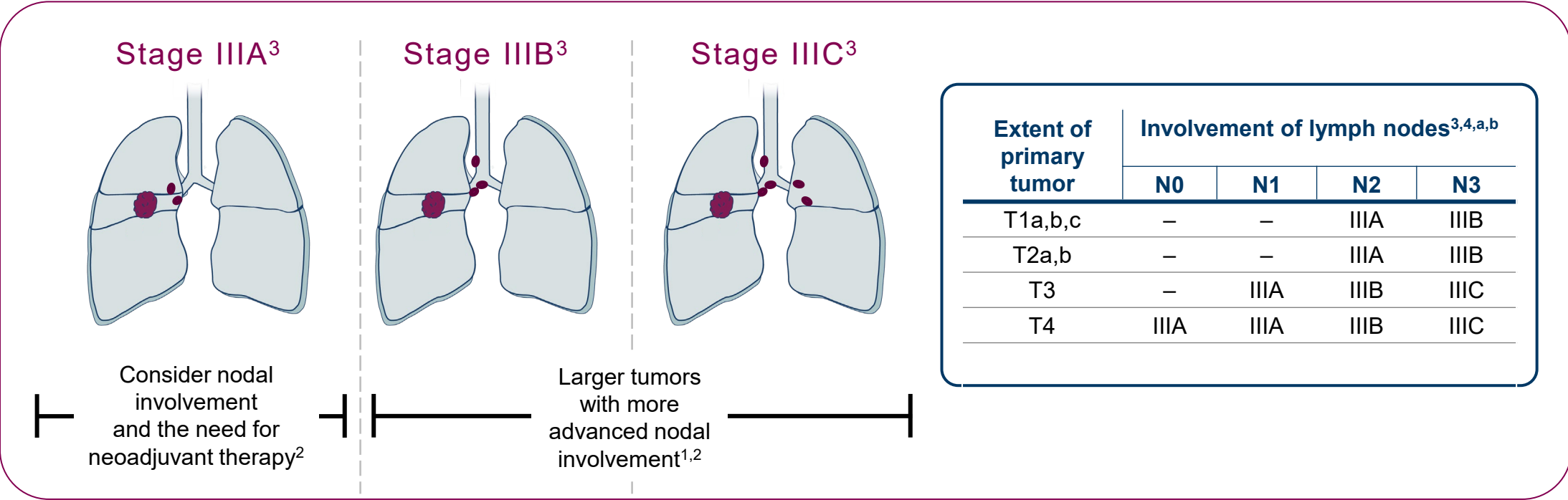
- This presentation is supported by AstraZeneca
 - This presentation is intended to provide educational information on the importance of MDT collaboration and care coordination for patients with early-stage NSCLC, and to review Stage II and/or Stage III NSCLC cases
 - This presentation does not discuss or promote any investigational or approved drugs and does not refer to drugs by their brand name or commercial entities
 - The information in this program is consistent with FDA guidelines, and the program is not CME accredited and may not be used for CME accreditation



Treatment and Management of Early-Stage NSCLC



Stage I and Stage II NSCLC Is Generally Considered Resectable, but Eligibility for Surgery Varies Across Stage III Disease^{1,2}



All possible combinations are not presented in these images.

^aStage I and II disease presentations are not included in this table. ^bBased on the 8th edition of the AJCC guidelines.

AJCC, American Joint Committee on Cancer; N, node; NSCLC, non-small cell lung cancer; T, tumor.

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NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Recommend Pretreatment Evaluation for Patients With Early-Stage NSCLC^a

Evaluate for perioperative therapy (Stage IB through Stage IIIB [T3, N2])

PFTs (if not previously done)

Bronchoscopy

Pathologic mediastinal lymph node evaluation^b

Brain MRI with contrast^{c,d}

MRI with contrast of spine + thoracic inlet for superior sulcus lesions abutting the spine, subclavian vessels, or brachial plexus^e

FDG-PET/CT scan^f (if not previously done)

^aUnless otherwise noted, these recommendations apply to patients with Stage IA through IIIB (T3, N2) disease and IIB-IIIA disease with separate pulmonary nodules. ^bMethods for evaluation include mediastinoscopy, mediastinotomy, EBUS, EUS, and CT-guided biopsy. An EBUS-TBNA negative for malignancy in a clinically (FDG-PET/CT and/or CT) positive mediastinum should undergo subsequent mediastinoscopy prior to surgical resection. ^cIf MRI is not possible, CT of head with contrast. ^dRecommended for patients with Stage II-IIIB (T3, N2) disease; optional for those with Stage IB disease. ^eRecommended for patients with Stage IIB (T3 invasion, N0) or Stage IIIA (T4 extension, N0-1; T3, N1; T4, N0-1) disease. ^fFDG-PET/CT performed skull base to mid-thigh. Positive FDG-PET/CT scan findings for distant disease need pathologic or other radiologic confirmation. If FDG-PET/CT scan is positive in the mediastinum, lymph node status needs pathologic confirmation.

CT, computed tomography; EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound; FDG-PET, fluorodeoxyglucose-positron emission tomography; MRI, magnetic resonance imaging; N, node; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; PFT, pulmonary function test; T, tumor; TBNA, transbronchial needle aspiration.

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Assessment of Technical Resectability and Medical Operability Helps Inform Treatment Modality Selection in Early-Stage NSCLC

Technical Resectability

Technical resectability is dependent on tumor-related factors^{1,2}

Potential resection outcomes include:

- Complete surgical resection (R0) with clear surgical margins being feasible
- Incomplete surgical resection (R1 and R2) with evidence of cancer remaining after surgery

Accurate preoperative **staging to determine the size, position, and invasiveness of the primary tumor and degree of nodal involvement** may potentially allow for **R0 resection¹⁻⁴**

Medical Operability

A patient who is deemed medically operable can tolerate surgery and there are acceptable postoperative risks¹

Medical operability evaluation typically includes assessment of¹:

- Age and performance status
- Comorbidities
- Extent of lymph node involvement
- Cardiac risk and pulmonary function

Medical operability evaluation helps to predict **postoperative function** and **quality of life¹**



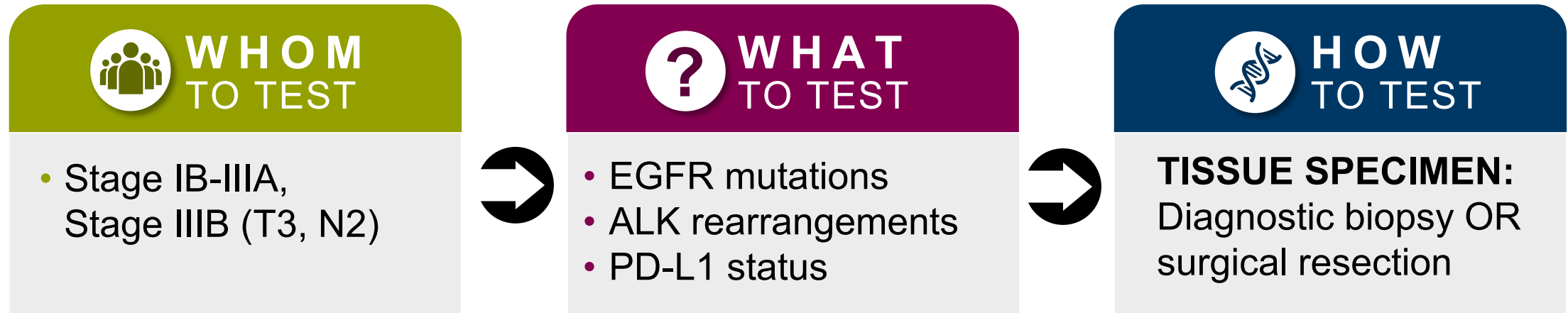
Expert Perspective: MDT Discussion



- In your practice, which specialists are typically involved in discussions of a patient's technical resectability and medical operability?
- What clinical characteristics do they typically weigh most heavily when determining resectability and operability?



NCCN Guidelines® Recommend Biomarker Testing for Patients With Early-Stage NSCLC^a



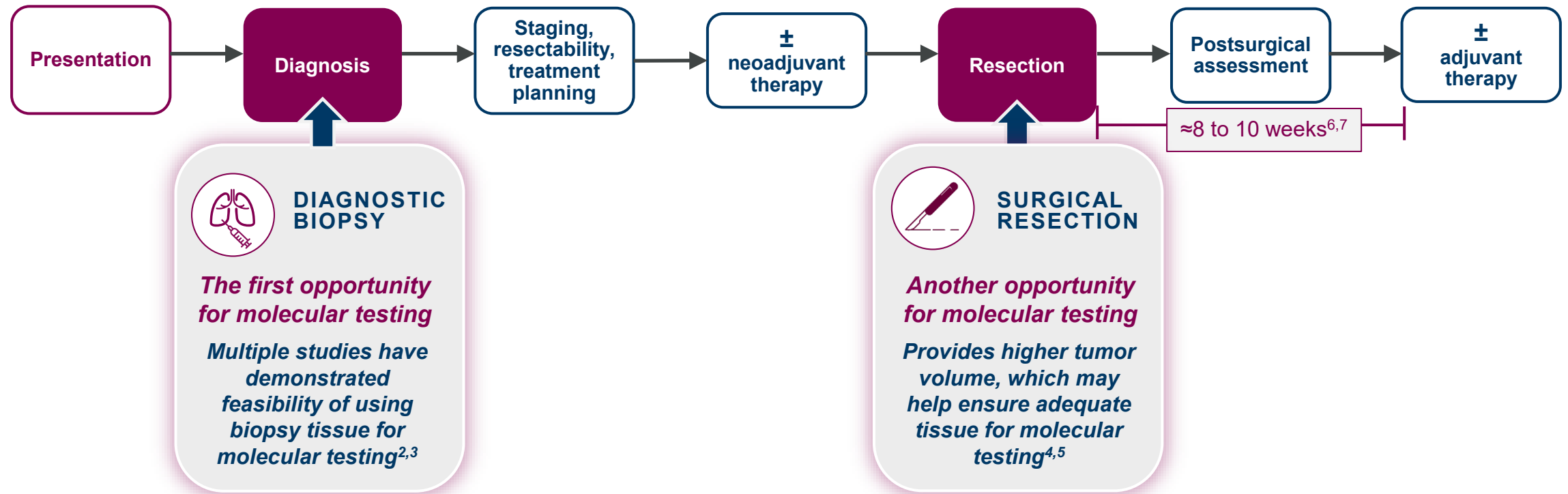
^aThe NCCN Guidelines for Non-Small Cell Lung Cancer provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.

ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; N, node; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; T, tumor.

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Opportunities for Biomarker Testing¹ Using an Example of a Patient Journey for Resectable NSCLC



Preoperative molecular testing using a biopsy sample is of growing importance, as treatment plans are starting to be made prior to surgery⁸

NSCLC, non-small cell lung cancer.

1. National Cancer Institute. Non-Small Cell Lung Cancer Treatment (PDQ®)—Health Professional Version. Accessed July 16, 2024. <https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq>.
2. Coley SM, et al. *Cancer Cytopathol.* 2015;123(5):318-326. 3. Schmid-Bindert G, et al. *PLoS One.* 2013;8(10):e77948. 4. Lim C, et al. *Curr Oncol.* 2017;24(2):103-110. 5. Aisner D, Marshall CB. *Am J Clin Pathol.* 2012;138(3):332-346. 6. Owen D, Chaft JE. *J Thorac Dis.* 2018;10(suppl 3):S404-S411. 7. Salazar MC, et al. *JAMA Oncol.* 2017;3(5):610-619. 8. Kidane B, et al. *J Thorac Cardiovasc Surg.* 2023;166(3):637-654.



Expert Perspective: MDT Discussion



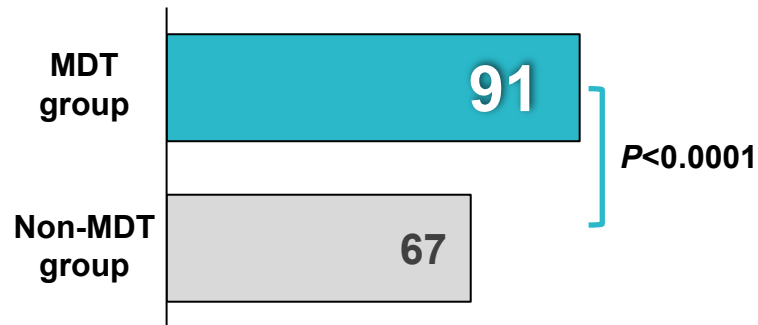
- **When do you typically initiate biomarker testing for your eligible patients with early-stage NSCLC?**
- **Which specialist(s) typically order testing? Do you have a standardized process?**
- **How do you proceed with biomarker testing in instances where the tumor sample is small, or insufficient tumor tissue is collected?**



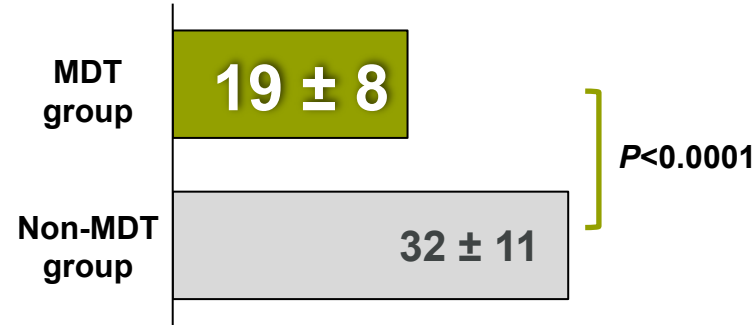
The MDT May Play a Crucial Role in Ensuring Optimal Treatment Planning and Outcomes for Patients With NSCLC

A retrospective analysis compared quality and cost of care outcomes for a cohort of 13,254 propensity-matched patients with Stage I-III NSCLC who were followed between 2008-2013, half of whom (N=6627) had prospective MDT care coordination and half of whom (N=6627) did not. The study found that the patients in the MDT group had:

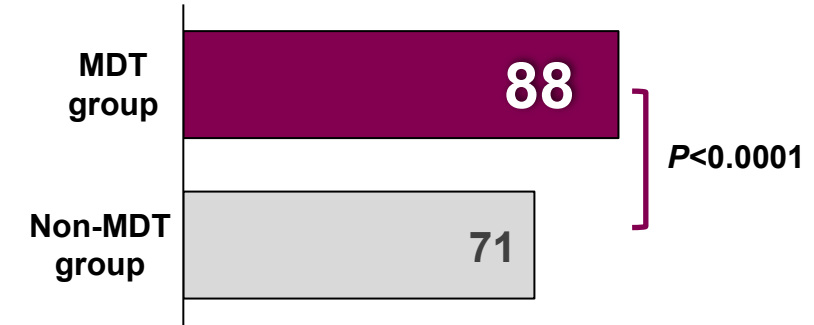
More Frequent Complete Staging Evaluations (%)^a



Shorter Time From Diagnosis to Treatment (Days)



Improved Adherence to Guideline-Based Treatment (%)



^aComplete Staging Evaluation included a minimum of a CT of the chest, including the upper abdomen and adrenal glands, endobronchial ultrasound /mediastinoscopy or positron emission tomography, or both, bronchoscopy, CBC, electrolyte profile, further evaluation of any specific symptoms and imaging specific for superior sulcus tumors when indicated.

CBC, complete blood count; CT, computed tomography; MDT, multidisciplinary team; NSCLC, non-small cell lung cancer.

Freeman RK, et al. *Ann Thorac Surg*. 2015;100(5):1834-1838.



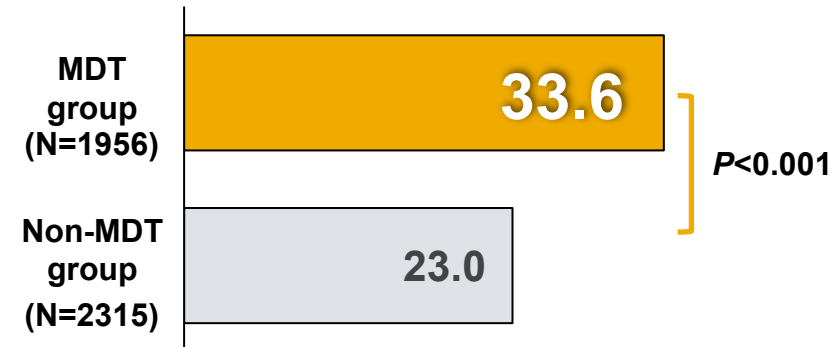
The MDT May Play a Crucial Role in Ensuring Optimal Treatment Planning and Outcomes^a for Patients With NSCLC (Cont'd)^{1,2}

Lower 3-Year Recurrence Rates¹

in patients with lung cancer enrolled in an MDT program (N=1179) compared to those not enrolled (N=865)

OR=0.51 (95% CI: 0.32-0.79)

Improved 5-Year OS Rates (%)²



Propensity-matched HR=0.65 (95% CI: 0.54-0.77)

^aTwo retrospective longitudinal analyses of data captured by the Stony Brook Cancer Center Registry compared health outcomes for patients with Stage I-Stage IV lung cancer (NSCLC, SCLC) who were or were not enrolled in an MDT program.^{1,2} A 10-year (2006-2015) analysis by Nemesure et al (2020) included 2044 patients from the Registry (MDT group, N=1179; non-MDT group, N=865).¹ A 15-year (2002-2016) analysis by Bilfinger et al (2018) included 4271 patients from the Registry (MDT group, N=1956; non-MDT group, N=2315).²

HR, hazard ratio; MDT, multidisciplinary team; NSCLC, non-small cell lung cancer; OR, odds ratio; OS, overall survival.

1. Nemesure B, et al. *Cancer Epidemiol.* 2020;68:101804. 2. Bilfinger TV, et al. *Clin Lung Cancer.* 2018;19(4):346-351.



Expert Perspective: MDT Discussion



- If you have an established MDT, how has implementing it impacted your practice workflow and NSCLC patient outcomes thus far?
- Are there any other changes you wish to see in the future?
- If you do NOT have an MDT, what would need to change in your practice/institution in order to establish one?



Case Scenario: Stage III NSCLC



Alan^a Presented to His PCP With a Prolonged Productive Cough



CASE DETAILS

Age and gender: **67-year-old male**

Smoking history: **Former smoker, 40 pack-year history**

Presenting symptom(s): **Prolonged productive cough that did not improve with OTC treatment**

Comorbidities: **Hypertension, asthma**

PS: **ECOG PS=1**

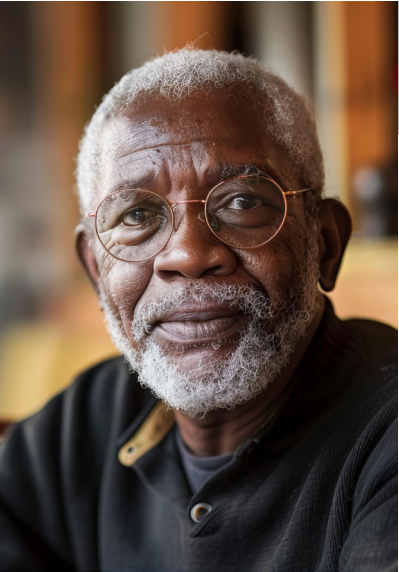
Imaging: **X-ray revealed a single mass in the lung concerning for malignancy**

Next steps: **The PCP referred Alan to a pulmonologist**

^aHypothetical patient profile.
ECOG, Eastern Cooperative Oncology Group; OTC, over-the-counter; PCP, primary care physician; PS, performance status.



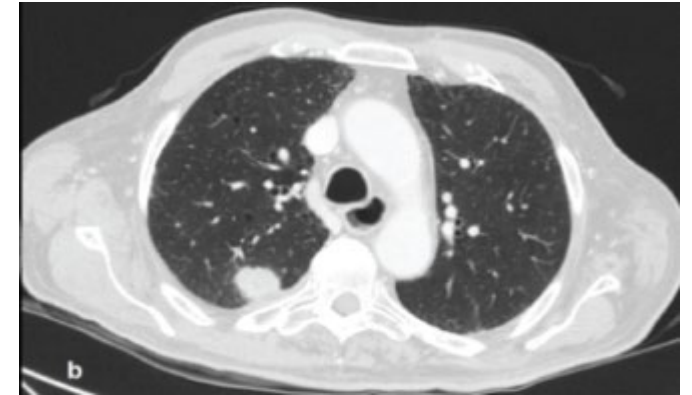
Alan's Pulmonologist Ordered a PET/CT and Performed PFTs and a Bronchoscopy



CASE DETAILS

PET/CT: CT: 5.2 × 3.1-cm mass in RUL of lung, invading chest wall

PET: SUVmax of primary mass=12.1; SUVmax of hilar node and mediastinal node=9.4 and 7.2, both suspicious for malignancy; no distant metastases



PFT results: DLCO 70%, FEV₁ 70%

Bronchoscopy with EBUS: Revealed multistation N2 disease (stations 4, 7 positive for malignancy)

Next steps: The pulmonologist referred Alan to a medical oncologist



Expert Perspective: MDT Discussion



- In your practice, what is the typical referral pattern for patients suspected of having NSCLC?
- Are there any other tests you would have ordered for Alan at this point in his care?



Alan's Medical Oncologist Diagnosed Him With EGFR/ALKwt Stage IIIB NSCLC



CASE DETAILS

Brain MRI: Negative for intracranial metastasis

Staging/histology: Stage IIIB (T3N2M0) NSCLC, nonsquamous adenocarcinoma

Biomarker results: EGFR/ALK negative, PD-L1=40%

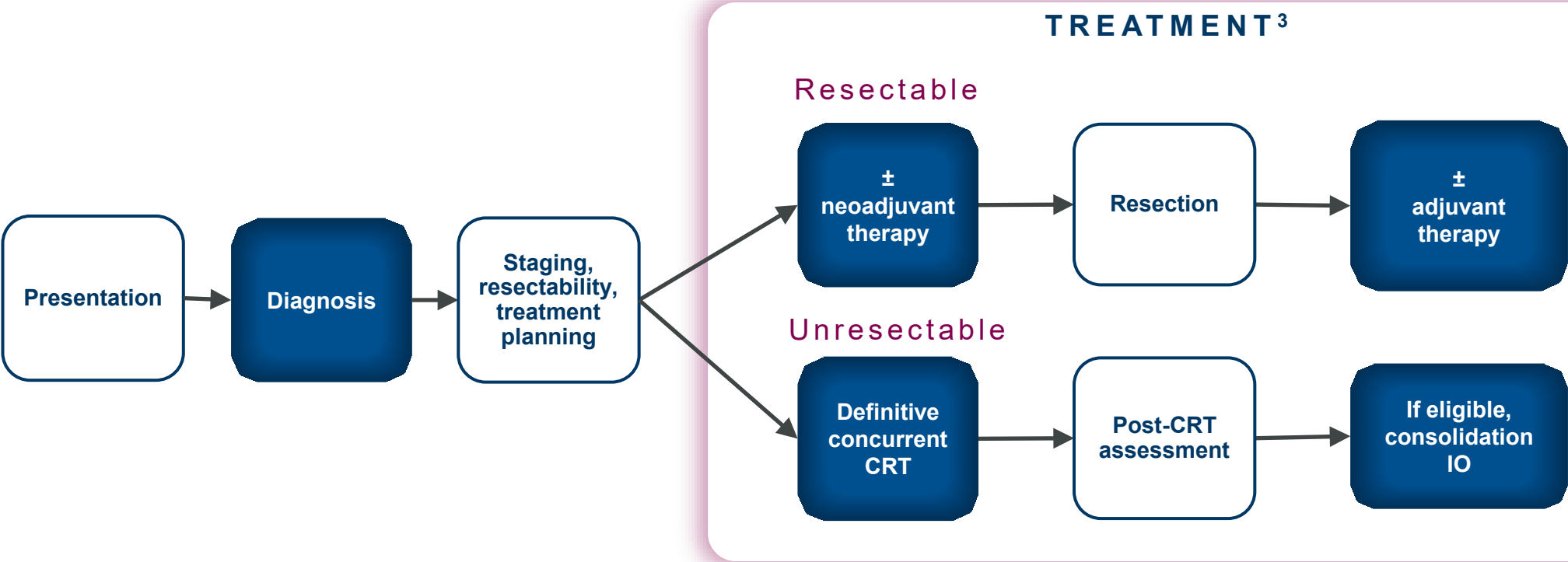
Next steps: The medical oncologist brought Alan's case to the tumor board to discuss technical resectability, medical operability, and to determine a treatment plan

ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; M, metastasis; MRI, magnetic resonance imaging; N, node; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; T, tumor; wt, wild-type.



An MDT Approach Helps to Ensure Guideline-Recommended Therapy for Patients With NSCLC¹

PATIENT JOURNEY EXAMPLE FOR STAGE III NSCLC²



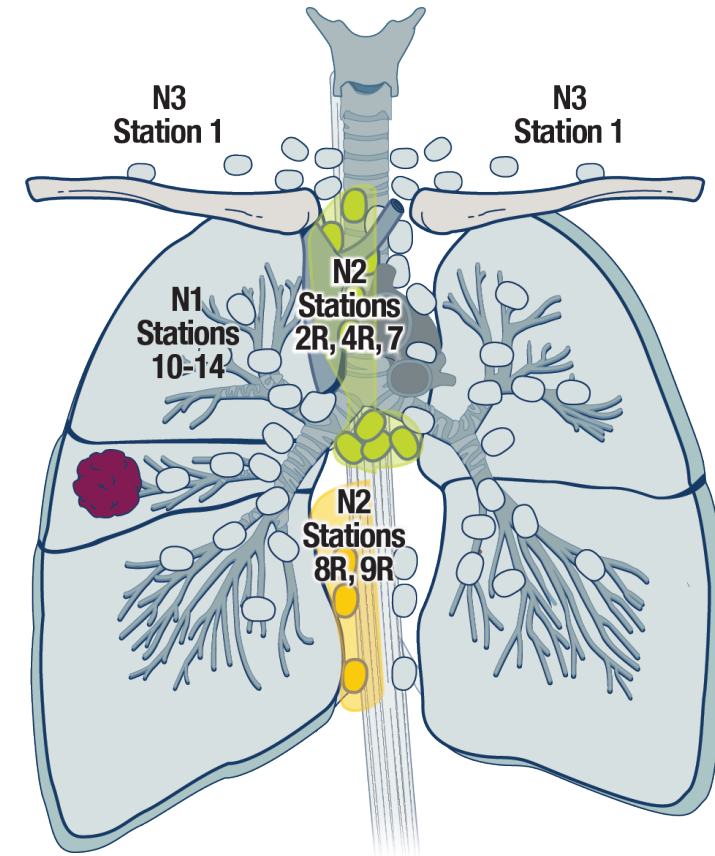
CRT, chemoradiation therapy; IO, immunotherapy; MDT, multidisciplinary team; NSCLC, non-small cell lung cancer.

1. Postmus PE, et al. *Ann Oncol*. 2017;28(suppl 4):iv1-iv21. 2. National Cancer Institute Non-Small Cell Lung Cancer Treatment (PDQ®)—Health Professional Version. Accessed September 25, 2024. <https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq>. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.10.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed September 25, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.



Management of N2 Disease Is Controversial and Requires a Multidisciplinary Team¹

- Lymph node involvement impacts resectability²
- Decisions regarding resectability should be evaluated within a multidisciplinary team¹ and should consider whether:
 - Nodes are bulky ($\approx >2$ cm)³
 - Tumors have spread beyond the nodal capsule²
 - There is multistation N2 disease⁴



N, node.

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EORTC Is Aiming to Build Consensus on Stage III NSCLC Resectability to Support Clinical Decision-Making^{a-c}

	N0	N1	N2 SINGLE-STATION	N2 MULTISTATION	N2 BULKY	N2 INVASIVE
T1-2	Not Stage III	Not Stage III	Potentially resectable	?	?	Unresectable
T3 SIZE	Not Stage III	Resectable	Potentially resectable	?	Unresectable	Unresectable
T3 SATELLITE	Not Stage III	Potentially resectable	Potentially resectable	?	Unresectable	Unresectable
T3 INVASION	Not Stage III	Potentially resectable	?*	?	Unresectable	Unresectable
T4 SIZE	Potentially resectable	Potentially resectable	?	?	Unresectable	Unresectable
T4 SATELLITE	Potentially resectable	?*	?	Unresectable	Unresectable	Unresectable
T4 INVASION	?*	?*	?	Unresectable	Unresectable	Unresectable

^aTable adapted from an international EORTC survey on resectability of Stage III NSCLC. ^bA question mark assigned to a TN combination indicates a lack of consensus (ie, <75% agreement) among the entire group of respondents. ^cThe 4 TN combinations denoted by a question mark and asterisk (“?*) were considered “potentially resectable” by survey respondents who are thoracic surgeons.

EORTC, European Organisation for Research and Treatment of Cancer; N, node; NSCLC, non-small cell lung cancer; T, tumor.

Houda I, et al. Presented at: International Association for the Study of Lung Cancer 2023 World Conference on Lung Cancer; September 10, 2023; Singapore: Abstract OA06.03.



Expert Perspective: MDT Discussion



- How do you typically manage patients with Stage III N2 disease?
- How have your treatment decisions for these patients changed over time?
- At this point in Alan's journey, is there any other information you/your team would need to know before making a decision on resectability?



Alan's MDT^a Discussed His Case at a Tumor Board

RADIOLOGIST

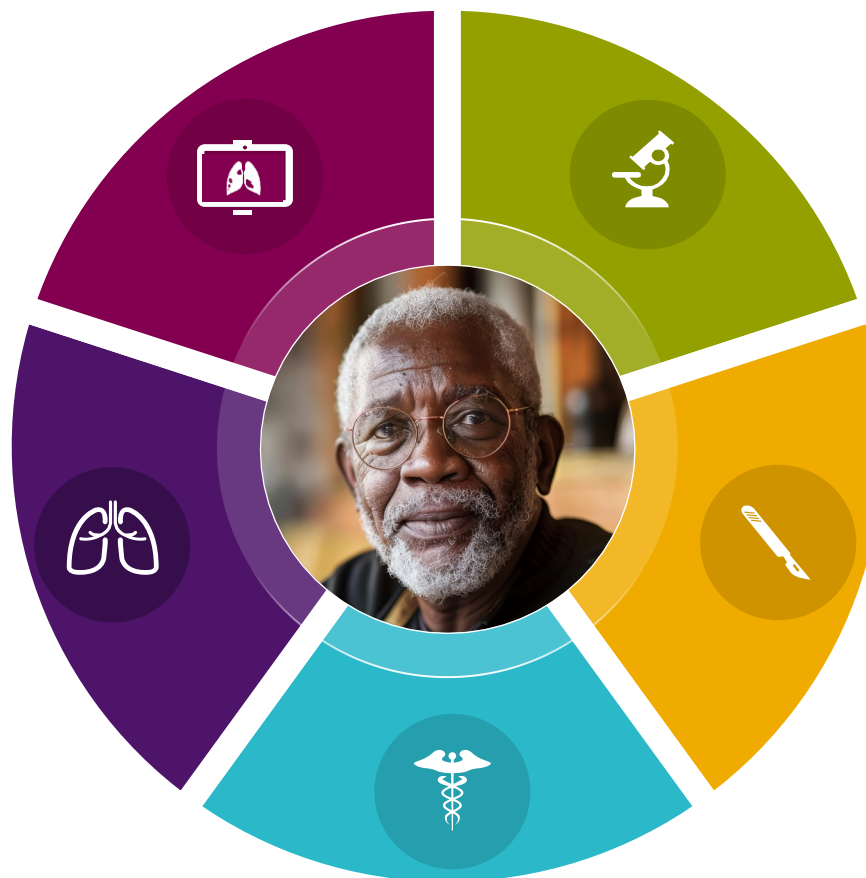
Reviewed imaging results
(brain MRI was negative
for metastases)

PATHOLOGIST

Presented histology (nonsquamous
adenocarcinoma) and noted that the
patient did not have any actionable
EGFR or ALK mutations

PULMONOLOGIST

Reviewed lung function
and PFTs; no cause for
concern



THORACIC SURGEON

Discussed Alan's medical operability
and technical resectability statuses.
ECOG PS and PFTs informed
operability, while the presence of
multistation N2 disease informed
tumor resectability. **Alan was
deemed medically operable but
technically unresectable**

MEDICAL ONCOLOGIST

Summarized Alan's diagnosis and final staging
(**Stage IIIB [T3N2M0] NSCLC**) and reviewed
NCCN Guidelines—recommended therapies

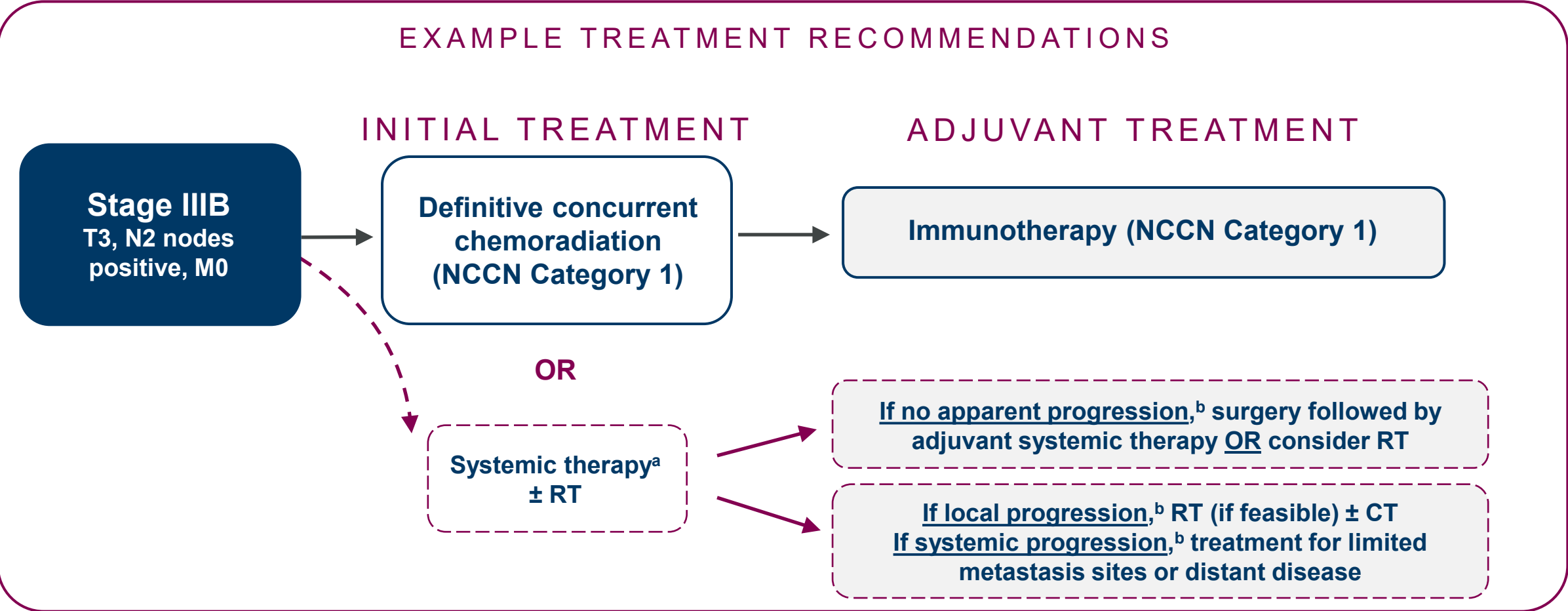
^aEvery MDT is different and the above does not necessarily include all relevant team members.

ALK, anaplastic lymphoma kinase; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; M, metastasis; MDT, multidisciplinary team; MRI, magnetic resonance imaging; N, node; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; PFT, pulmonary function test; PS, performance status; T, tumor.

Hardavella G, et al. *Breathe*. 2020;16(4):200076.



NCCN Guidelines Recommendations: Initial and Adjuvant Treatment Options for Stage IIIB (T3N2M0) NSCLC



^aSelected patients with N2 disease (fit, single-station, non-bulky N2, requiring only lobectomy) may be considered for systemic therapy followed by surgery. ^bChest CT with contrast and/or FDG-PET/CT to evaluate progression.

ALK, anaplastic lymphoma kinase; CT, chemotherapy; EGFR, epidermal growth factor receptor; FDG, fludeoxyglucose-18; M, metastasis; N, node; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; PET/CT, positron emission tomography/computed tomography; RT, radiation therapy; T, tumor; wt, wild-type.

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Expert Perspective: MDT Discussion



- In your practice, when are radiation oncologists and thoracic surgeons brought into treatment/management conversations for patients with Stage III NSCLC?
- How do medical and radiation oncologists typically coordinate care and monitoring for NSCLC progression after CRT/prior to starting IO?
- How might you discuss a treatment plan with Alan and his caregiver(s)?
- What concerns do patients typically raise during these conversations? How do you respond to these concerns?



Case Scenario: Stage II NSCLC



Nancy^a Presented With a Severe Nonproductive Cough During a Consultation With Her PCP



CASE DETAILS	
Age and gender:	68-year-old female
Smoking history:	Former smoker (10 pack-years, discontinued 20 years ago)
Presenting symptom(s):	Severe nonproductive cough, unresponsive to 2 rounds of antibiotics, dyspnea on exertion
Comorbidities:	Hypertension, asthma
PS:	ECOG PS=1
Next steps:	Nancy's PCP ordered a PET/CT scan and referred her to a pulmonologist for evaluation

^aHypothetical patient profile.
ECOG, Eastern Cooperative Oncology Group; PCP, primary care physician; PET/CT, positron emission tomography/computed tomography; PS, performance status.



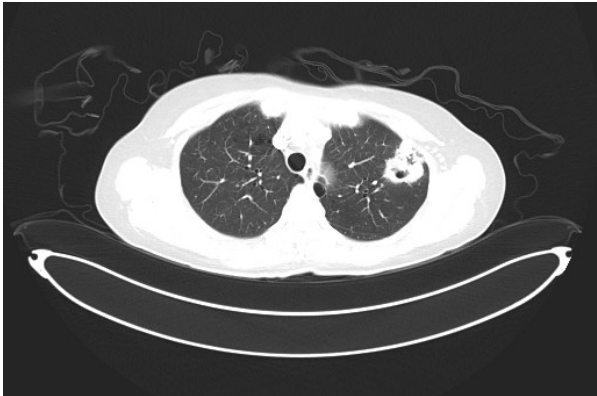
Nancy's Pulmonologist Reviewed the PET/CT Results and Performed PFTs and a Bronchoscopy



CASE DETAILS

PET/CT: CT: 4.5 × 5.1-cm cavitating mass in LUL of lung

PET: SUVmax of primary mass=6.5; SUVmax of hilar node=2.2, suspicious for malignancy; no distant metastases



PFT results: DLCO 80%, FEV₁ 80%

Bronchoscopy with EBUS: No mediastinal involvement; 10L node was biopsied and found to be negative

Next steps: The pulmonologist sent the remaining biopsy sample to a pathologist and referred Nancy to a medical oncologist, who ordered a brain MRI and scheduled a tumor board meeting



Nancy's MDT^a Discussed Her Case at a Tumor Board

RADIOLOGIST

Reviewed imaging results
(brain MRI was negative
for metastases)

PATHOLOGIST

Presented histology
(nonsquamous adenocarcinoma)
and informed the team that
biomarker testing was not
performed due to insufficient
tumor sample

PULMONOLOGIST

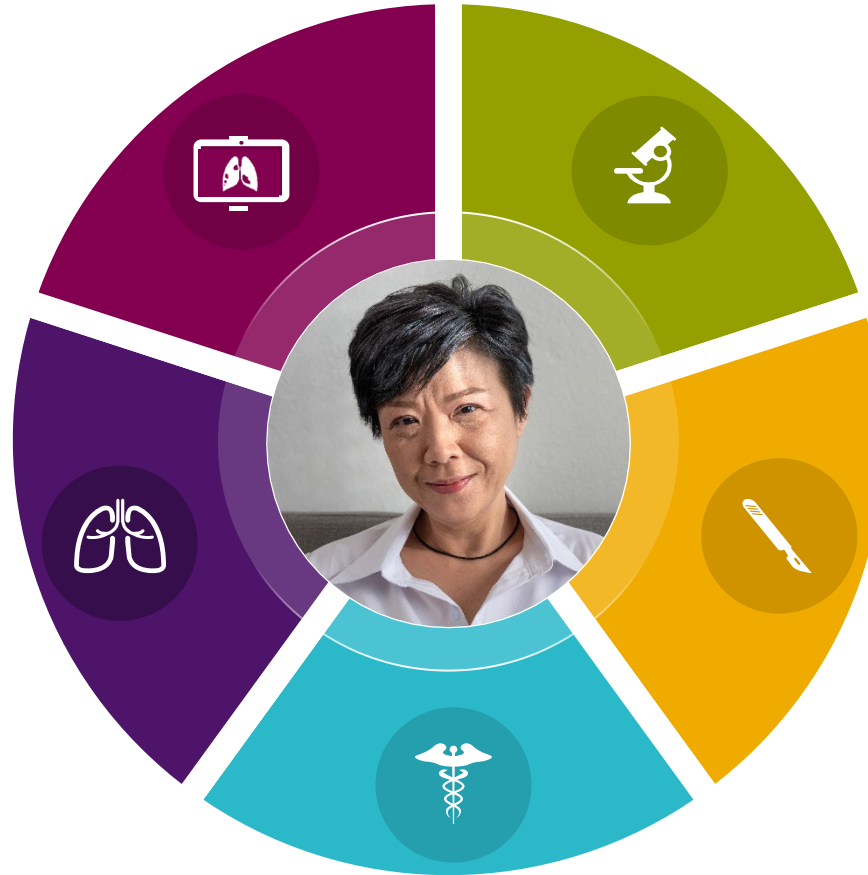
Reviewed lung function
and PFTs; no cause for
concern

THORACIC SURGEON

Discussed Nancy's medical operability
and technical resectability statuses.
ECOG PS and PFTs informed
operability, while the lack of mediastinal
involvement and presence of N1
disease informed resectability. **Nancy
was deemed medically operable and
her tumor resectable via lobectomy**

MEDICAL ONCOLOGIST

Summarized Nancy's diagnosis and final staging
(**Stage IIB [T3N0M0] NSCLC**) and reviewed NCCN
Guidelines—recommended therapies



^aEvery MDT is different and the above does not necessarily include all relevant team members.

ECOG, Eastern Cooperative Oncology Group; M, metastasis; MDT, multidisciplinary team; MRI, magnetic resonance imaging; N, node; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; PFT, pulmonary function test; PS, performance status; T, tumor.

Hardavella G, et al. *Breathe*. 2020;16(4):200076.

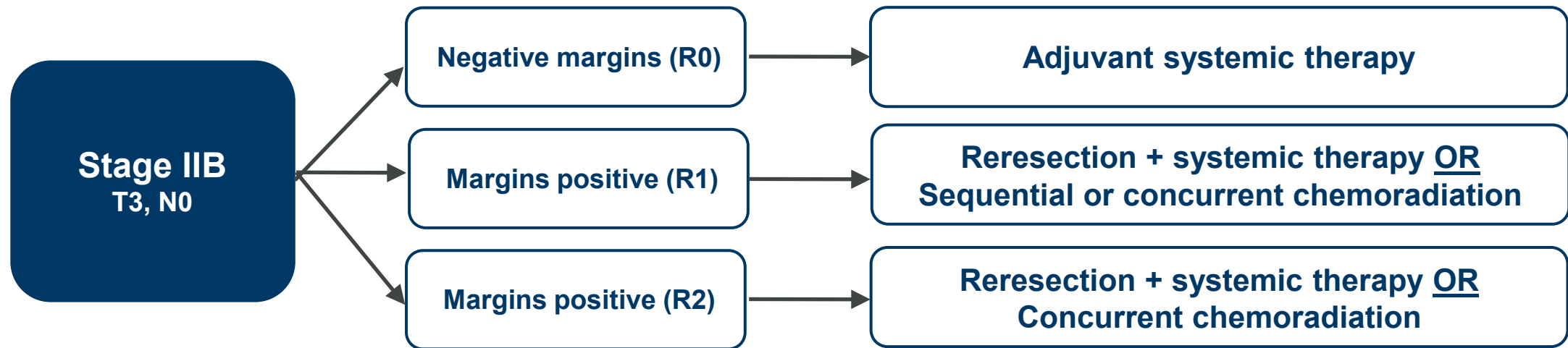


NCCN Guidelines Recommendations for Medically Operable and Technically Resectable Stage IIB (T3N0M0) NSCLC

INITIAL TREATMENT

- Neoadjuvant IO + CT should be strongly considered for patients who are eligible for IO and have tumors ≥ 4 cm or have positive LNs
- Surgical exploration and resection + mediastinal LN dissection or systemic LN sampling after preoperative systemic therapy, if planned

ADJUVANT TREATMENT



CT, chemotherapy; IO, immunotherapy; LN, lymph node; N, node; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; R0, zero residual tumor; R1, microscopic residual tumor; R2, macroscopic residual tumor; T, tumor.

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Expert Perspective: MDT Discussion



- How might you proceed with a treatment plan when a patient's biomarker status is unknown? Would you perform a repeat biopsy to obtain more tissue?
- When recommending a surgical approach, might you consider adding neoadjuvant treatment or plan for perioperative treatment?
 - Which clinical factors weigh most heavily on the decision to use these modalities?
- If Nancy were to undergo resection, how might you proceed with adjuvant treatment if she were to achieve R0 vs R1 vs R2 status?





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This concludes our presentation.



Q&A



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