Inside the Issue: Integrating Targeted and Immunotherapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, September 21, 2023 5:00 PM – 6:00 PM ET

Faculty Jamie E Chaft, MD John V Heymach, MD, PhD



Faculty



Jamie E Chaft, MD Associate Attending Physician Thoracic Oncology Service Memorial Sloan Kettering Cancer Center New York, New York



Moderator Neil Love, MD Research To Practice



John V Heymach, MD, PhD

Professor and Chair Thoracic/Head and Neck Medical Oncology The University of Texas MD Anderson Cancer Center Houston, Texas



Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP and Merck.



Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.



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Dr Chaft — Disclosures

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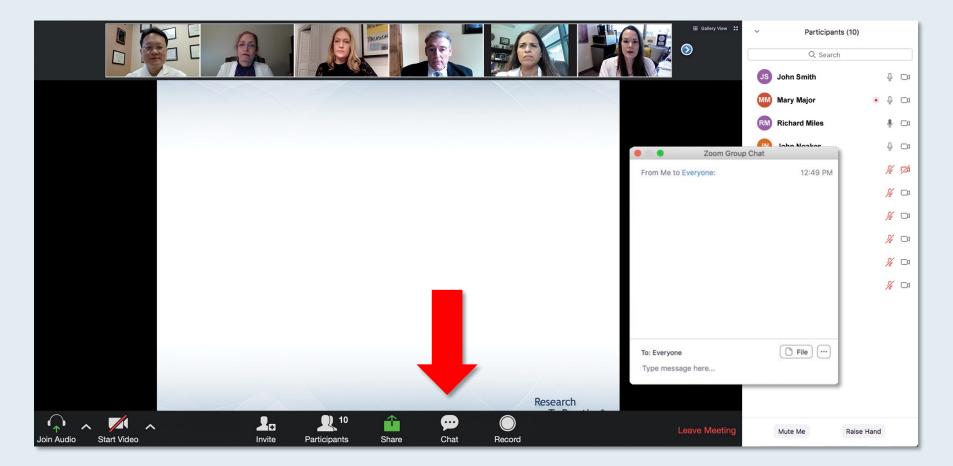


Dr Heymach — Disclosures

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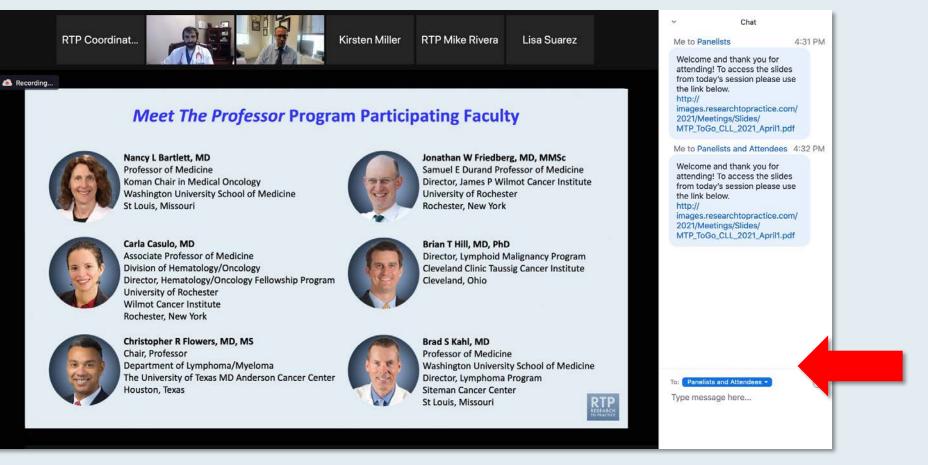


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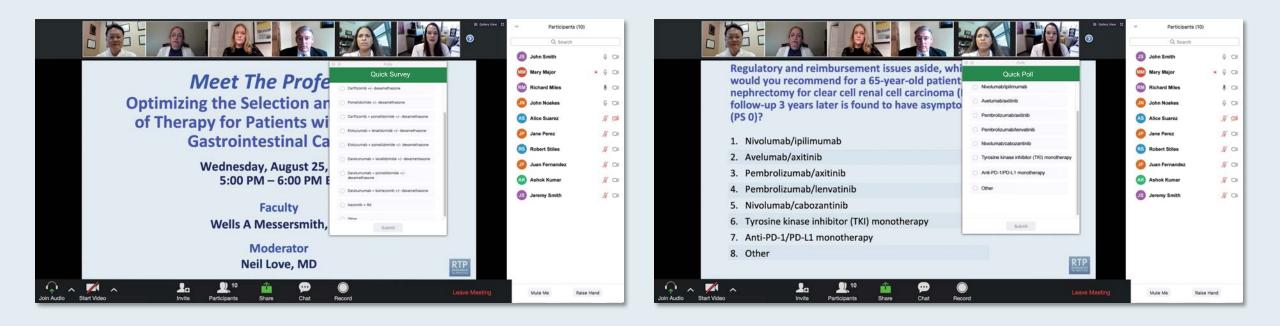
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Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys





ONCOLOGY TODAY WITH DR NEIL LOVE

Special Edition — Key Presentations on Lung Cancer from the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting



DR MATTHEW GUBENS UNIVERSITY OF CALIFORNIA, SAN FRANCISCO









Dr Matthew Gubens – Special Edition -Oncology Today with Dr Neil Love —

(15) (30)

What Clinicians Want to Know About the Management of Relapsed/Refractory Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Tuesday, September 26, 2023 5:00 PM – 6:00 PM ET

Faculty Toby A Eyre, MBChB, DipMedEd, MRCP, MD Brad S Kahl, MD



Meet The Professor Optimizing the Management of Gastroesophageal Cancers

> Thursday, September 28, 2023 5:00 PM – 6:00 PM ET

> > Faculty Peter C Enzinger, MD



Inside the Issue: Optimizing the Management of Nonmelanoma Skin Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, October 3, 2023 5:00 PM – 6:00 PM ET

Faculty Nikhil I Khushalani, MD Anna C Pavlick, DO, MBA



Current Approaches and Future Strategies in Oncology A Multitumor Educational Symposium in Partnership with Florida Cancer Specialists & Research Institute Saturday, October 7, 2023

ER-Positive Breast Cancer 7:15 AM – 8:15 AM ET Faculty

Harold J Burstein, MD, PhD Komal Jhaveri, MD Prostate Cancer 8:15 AM – 9:15 AM ET Faculty

Alicia K Morgans, MD, MPH Matthew R Smith, MD, PhD

Moderator

Neil Love, MD



Current Approaches and Future Strategies in Oncology A Multitumor Educational Symposium in Partnership with Florida Cancer Specialists & Research Institute

Saturday, October 7, 2023

Non-Small Cell Lung Cancer 9:30 AM – 10:30 AM ET

Faculty

Gregory J Riely, MD, PhD Heather Wakelee, MD, FASCO Colorectal and Gastroesophageal Cancers 10:30 AM – 11:30 AM ET

Faculty

Tanios Bekaii-Saab, MD Philip A Philip, MD, PhD, FRCP



Current Approaches and Future Strategies in Oncology A Multitumor Educational Symposium in Partnership with Florida Cancer Specialists & Research Institute Saturday, October 7, 2023

Chronic Lymphocytic Leukemia 11:30 AM – 12:30 PM ET

Faculty

Asher Chanan-Khan, MD

Brad S Kahl, MD

Moderator

Neil Love, MD



Oncology in the Real World A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network Saturday, October 14, 2023

Lymphoma 9:30 AM – 10:30 AM PT (12:30 PM – 1:30 PM ET)

Faculty

Christopher R Flowers, MD, MS Ann S LaCasce, MD, MMSc Urothelial Bladder Cancer and Renal Cell Carcinoma 10:30 AM – 11:30 AM PT (1:30 PM – 2:30 PM ET)

Faculty

Thomas E Hutson, DO, PharmD Guru P Sonpavde, MD



Oncology in the Real World A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network Saturday, October 14, 2023

Hepatobiliary and Pancreatic Cancers 11:50 AM – 12:50 PM PT (2:50 PM – 3:50 PM ET)

Faculty

Mitesh J Borad, MD Anthony El-Khoueiry, MD **Gynecologic Cancers** 1:30 PM – 2:30 PM PT (4:30 PM – 5:30 PM ET)

Faculty

Bradley J Monk, MD Kathleen N Moore, MD, MS



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Multiple Myeloma 2:30 PM – 3:30 PM PT (5:30 PM – 6:30 PM ET)

Faculty

Amrita Krishnan, MD Robert Z Orlowski, MD, PhD HER2-Positive and Triple-Negative Breast Cancer 3:50 PM – 4:50 PM PT (6:50 PM – 7:50 PM ET)

Faculty

Sara A Hurvitz, MD, FACP Heather McArthur, MD, MPH



Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.



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John V Heymach, MD, PhD

Professor and Chair Thoracic/Head and Neck Medical Oncology The University of Texas MD Anderson Cancer Center Houston, Texas



Survey Participants



Mark Awad, MD, PhD Clinical Director, Lowe Center for Thoracic Oncology Dana-Farber Cancer Institute Assistant Professor of Medicine Harvard Medical School Boston, Massachusetts



Ramaswamy Govindan, MD Professor of Medicine Director, Section of Oncology Anheuser-Busch Endowed Chair in Medical Oncology Washington University School of Medicine St Louis, Missouri



Patrick Forde, MD

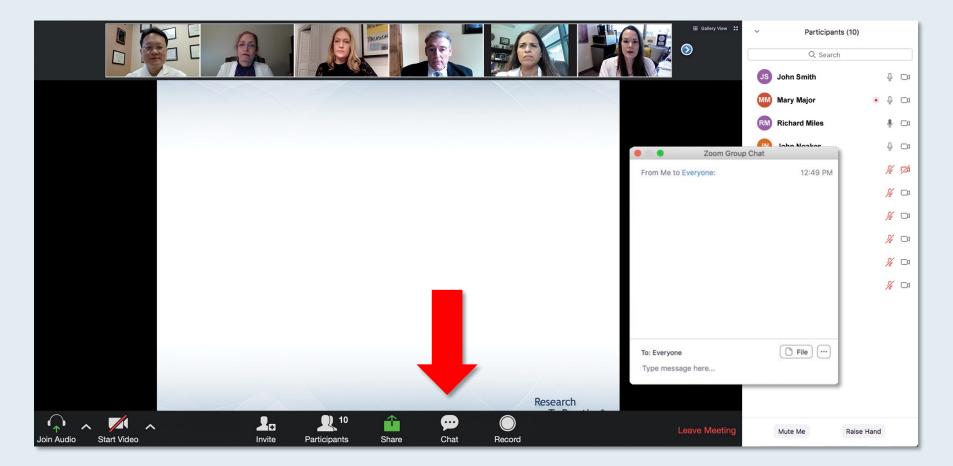
Co-Director, Division of Upper Aerodigestive Malignancies Associate Professor of Oncology Johns Hopkins University Baltimore, Maryland



Heather Wakelee, MD, FASCO Professor of Medicine Chief, Division of Oncology Deputy Director Stanford Cancer Institute President, International Association for the Study of Lung Cancer (IASLC) Stanford, California



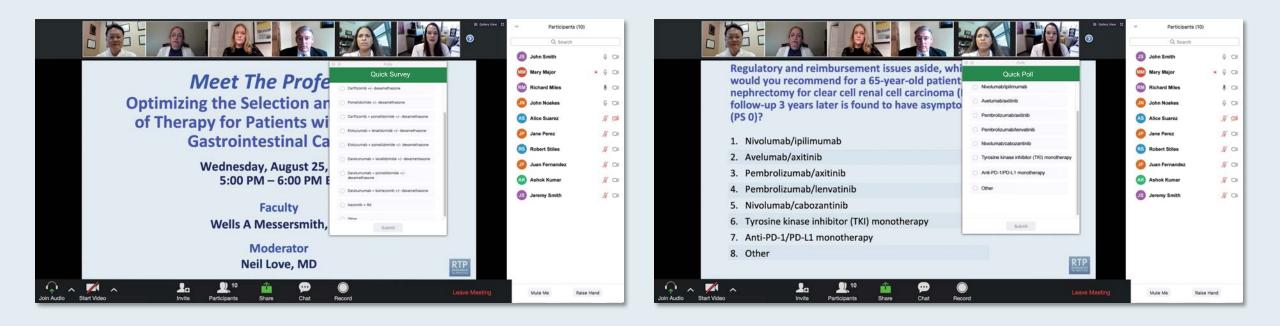
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Dr Chaft — Disclosures

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Dr Heymach — Disclosures

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Novel Approaches to Adjuvant Treatment for Localized NSCLC

John Heymach MD, PhD Chair, Thoracic/Head and Neck Medical Oncology David Bruton, Jr. Chair in Cancer Research MD Anderson Cancer Center

Research To Practice

Sept. 15, 2023



Memorial Sloan Kettering Cancer Center

The Evolving Role of Neoadjuvant Therapy for Localized Non-Small Cell Lung Cancer

September 18, 2023 Jamie <u>Chaft</u> www.MSKCC.org

> Memorial Sloan Kettering Cancer Center

MDAnderson Cancer Center

Making Cancer History"

cer Center

O PRACTIC

Key Data Sets

John V Heymach, MD, PhD

- Felip E et al. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIA nonsmall-cell lung cancer (IMpower010): A randomised, multicentre, open-label, phase 3 trial. *Lancet* 2021 October 9;398(10308):1344-57.
- Felip E et al. Overall survival with adjuvant atezolizumab after chemotherapy in resected stage II-IIIA non-small-cell lung cancer (IMpower010): A randomised, multicentre, open-label, phase III trial. Ann Oncol 2023 July 17;[Online ahead of print].
- Paz-Ares L et al. Pembrolizumab (pembro) versus placebo for early-stage non-small cell lung cancer (NSCLC) following complete resection and adjuvant chemotherapy (chemo) when indicated: Randomized, triple-blind, phase III EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 study. *Annals Oncology* 2022;33(4):451-3.
- O'Brien M et al. Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): An interim analysis of a randomised, triple-blind, phase 3 trial. *Lancet Oncol* 2022 October;23(10):1274-86.



Key Data Sets

John V Heymach, MD, PhD (continued)

- Chang JY et al. Stereotactic ablative radiotherapy with or without immunotherapy for earlystage or isolated lung parenchymal recurrent node-negative non-small-cell lung cancer: An open-label, randomised, phase 2 trial. *Lancet* 2023 September 9;402(10405):871-81.
- Wu Y-L et al. Osimertinib in resected EGFR-mutated non-small-cell lung cancer. *N Engl J Med* 2020;383:1711-23.
- Tsuboi M et al. Overall survival with osimertinib in resected EGFR-mutated. N Engl J Med 2023 July 13;389(2):137-47.
- Solomon BJ et al. ALINA: A phase III study of alectinib versus chemotherapy as adjuvant therapy in patients with stage IB-IIIA anaplastic lymphoma kinase-positive (ALK+) non-small cell lung cancer (NSCLC). ASCO 2019;Abstract TPS8569.



Key Data Sets

Jamie E Chaft, MD

- Girard N et al. Neoadjuvant nivolumab (N) + platinum-doublet chemotherapy (C) for resectable NSCLC: 3-y update from CheckMate 816. ELCC 2023;Abstract 84O.
- Wakelee H et al. KEYNOTE-671: Randomized, double-blind, phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early stage NSCLC. ASCO 2023;Abstract LBA100.
- Wakelee H et al. Perioperative pembrolizumab for early-stage non-small-cell lung cancer. *N Engl J Med* 2023 August 10;389(6):491-503.
- Heymach JV et al. AEGEAN: A phase 3 trial of neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in patients with resectable NSCLC. AACR 2023;Abstract CT005.
- Forde PM et al. nivolumab plus chemotherapy in resectable lung cancer. *N Engl J Med* 2022 May 26;386(21):1973-85.
- NeoADAURA: A study of osimertinib with or without chemotherapy versus chemotherapy alone as neoadjuvant therapy for patients with EGFRm positive resectable non-small cell lung cancer. NCT04351555



Agenda

INTRODUCTION: Patient Involvement in (Neo)Adjuvant Treatment Decisions

MODULE 1: Targetable Treatment in Localized Disease

MODULE 2: Immunotherapy in Localized Disease



Agenda

INTRODUCTION: Patient Involvement in (Neo)Adjuvant Treatment Decisions

MODULE 1: Targetable Treatment in Localized Disease

MODULE 2: Immunotherapy in Localized Disease



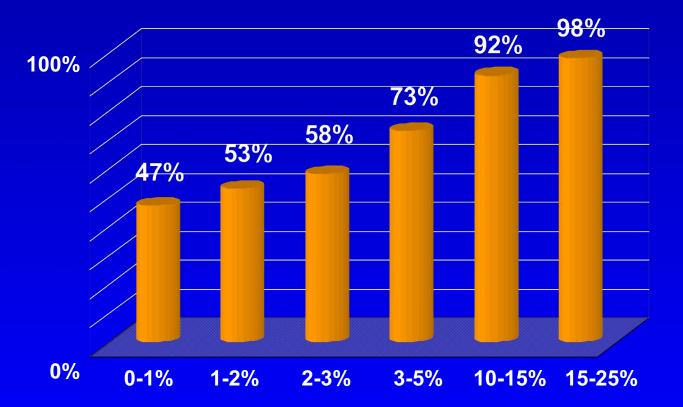
HOW WELL DO WE COMMUNICATE WITH OUR PATIENTS?

A Survey of Patients Who Received Adjuvant Chemotherapy for Colorectal Cancer

Neil Love, MD; Carma Bylund, PhD; Neal J Meropol, MD; John Marshall, MD; Steven A Curley, MD; Lee M Ellis, MD; Axel Grothey, MD; Heinz-Josef Lenz, MD; Leonard B Saltz, MD; Melanie Elder, BBA; Kathryn Ault Ziel, PhD; Douglas Paley, BA; Ginelle Suarez, BS; Erin Wall, BS

Australian Breast Cancer Patient Preference Study

What benefit would you require to receive chemotherapy?



Mortality Reduction Needed to Accept Adjuvant Chemotherapy

Sources: J Natl Cancer Inst Monogr 2001;30:146-52. Williams CJ, editor. Introducing new treatments for cancer: Practical, ethical and legal problems. London (UK): Wiley; 1992. p 447–58. Simes J, Coates AS. Intl Cancer Institute Monograph 2001;30:146-52.

Trade-Off Situations Presented After Review of Audio Program

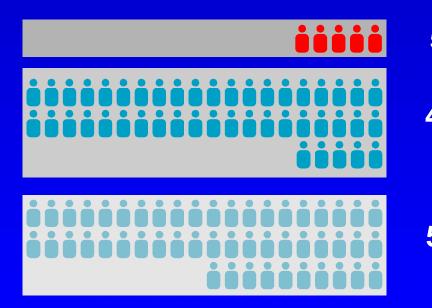
	Recurrence Risk		
Scenario	Baseline	With Chemotherapy	Absolute Benefit
1	50%	49%	1%
2	20%	19%	1%
3	20%	17%	3%
4	50%	45%	5%
5	20%	15%	5%
6	50%	40%	10%

Graphic Presentation of Scenarios

Scenario 4

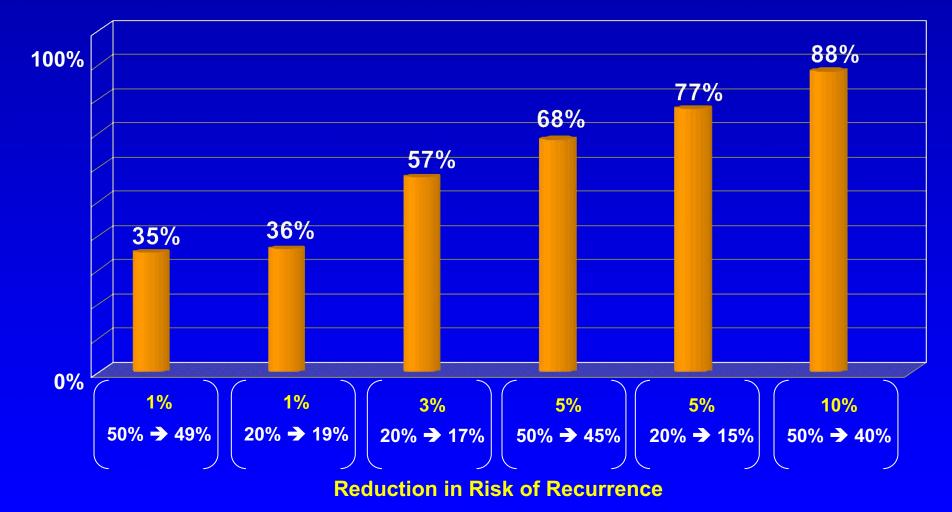
- Baseline recurrence risk: 50%
- Risk with chemotherapy: 45%

Would you receive treatment again?



- 5 Patients cured because of adjuvant chemotherapy
- 45 ← Patients whose cancer would return even though they received adjuvant chemotherapy

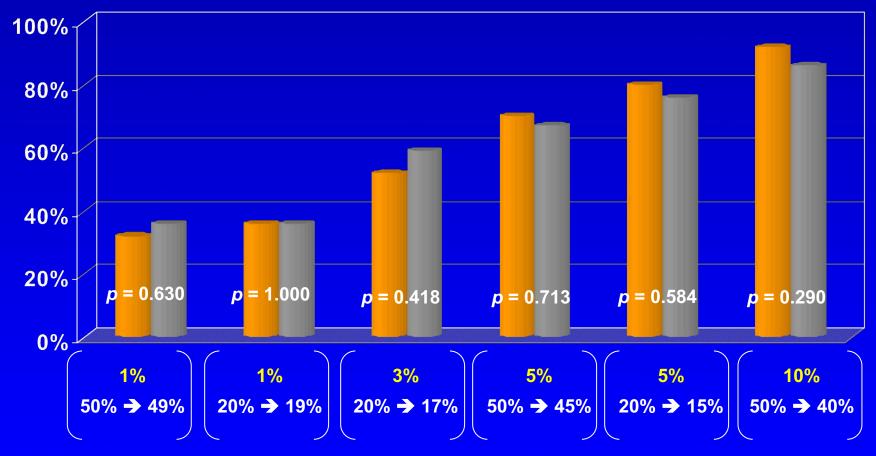
Percent of Patients Who Would be Treated Again for Various Reductions in Risk of Recurrence



Survey of 150 patients with colorectal cancer: 2006

Percent of Patients Who Would be Treated Again for Various Reductions in Risk of Recurrence

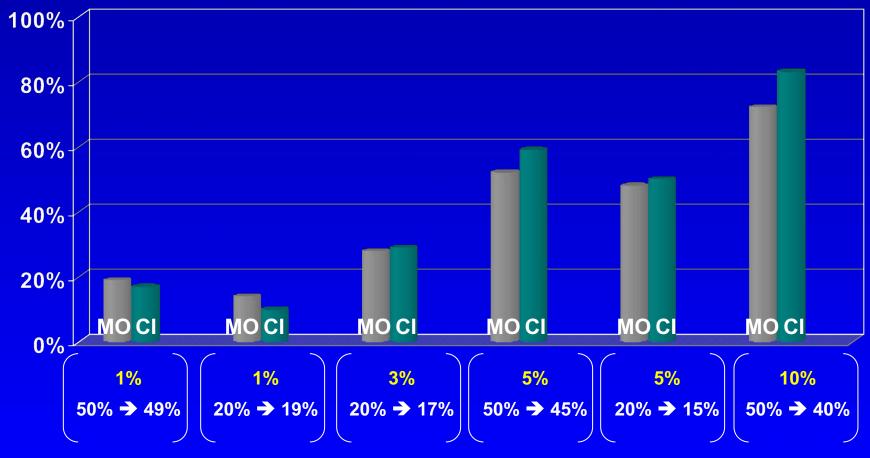
Male Female



Reduction in Risk of Recurrence

Male: n = 50; *female: n* = 100

Predictions of Patient Trade-Offs (Medical Oncologists and Clinical Investigators)



Reduction in Risk of Recurrence

Survey of 150 practicing oncologists: 2006

RTP CRC Patient Project Findings Publicized Nationally

USA TODAY · MONDAY, JANUARY 22, 2007 · 5D

Study: Doctors out of sync with cancer patients' wishes

By Liz Szabo **USA TODAY**

tients and their doctors.

presented Sunday at the 2007 ing with technical medical terms. Gastrointestinal Cancers Sympowilling to undergo chemotherapy, was very small.

Researchers posed a hypothetical question to patients who had al- colorectal cancer researcher at ready been treated with surgery New York's Memorial Sloan-Ketterand drugs: Would they again have ing Cancer Center, noted that the chemo – which can cause diarrhea, study had important limitations. nausea and crushing fatigue – if it Patients who answered the survey cut the risk of relapse by 1%? About may be more positive about chemo 35% said they would.

judging patients' responses, the they are probably already leaning in survey shows. Of 150 interviewed, that direction," Saltz says. only 19% of doctors and 17% of researchers thought patients tients before they have chemo. Sawould agree, says Neil Love, the nofi-Aventis, which makes cancer study's lead author and president drugs, paid for the survey.

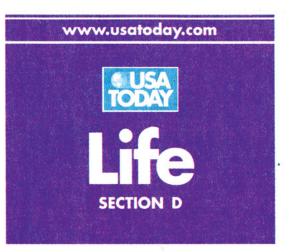
of a Miami medical education company called Research to Practice.

It's easy to understand why doc-ORLANDO - A new study sheds tors and patients don't always comlight on the hardships that cancer municate well, says Neal Meropol, patients are willing to endure in the director of gastrointestinal cancer hope of a cure – as well as the at Philadelphia's Fox Chase Cancer communication gap between pa- Center. Overwhelmed patients may not be able to concentrate during In a study of 150 patients office visits, especially when deal-

The study revealed other comsium, researchers found that many munication gaps, Love says. About colorectal cancer patients were 60% of patients say they weren't given the chance to join a clinical even when the potential benefit trial. Yet 81% wished they had gotten such information.

Leonard Saltz, a co-author and than others. "They had already had Doctors weren't very good at chemo and lived to tell about it, so

Love now plans to interview pa-



Monday, January 22, 2007

Would you say yes to chemotherapy?

Most doctors underestimated patients' willingness to take harsh therapies in exchange for a greater chance of remaining cancer-free.

> = Patients who said yes = Doctors who predicted patients would say ves

Would you get chemo if it cut		Yes
your risk of relapse from 50% to	49%	35% 19%
	45%	68% / 52%
Source: Neil Love, 2007 Gastrointestinal Cancers Symposium	40%	88% 72%



Regulatory and reimbursement issues aside, in general, which adjuvant treatment would you recommend for an otherwise healthy 65-year-old patient with <u>Stage IIA</u> nonsquamous NSCLC with an EGFR exon 19 deletion and a PD-L1 TPS of 50%? What would you estimate to be the approximate risk of recurrence if the patient <u>did versus did not receive adjuvant therapy</u>?

	Adjuwant treatment	Risk of recurrence	
	Adjuvant treatment	Without treatment	With treatment
Dr Chaft	Osimertinib	45%	15%
Dr Heymach	Chemotherapy → osimertinib	30%	10%
Dr Awad	Chemotherapy → osimertinib	35%	20%
Dr Forde	Chemotherapy → osimertinib	40%	10%
Dr Govindan	Chemotherapy → osimertinib	30%	20%
Dr Wakelee	Chemotherapy → osimertinib	70%	20%

Regulatory and reimbursement issues aside, which of the following would you most likely recommend as adjuvant therapy for a patient with completely resected Stage IIB lung adenocarcinoma and an EGFR-activating mutation? What would you estimate to be the approximate risk of recurrence if the patient <u>did versus did not receive adjuvant therapy</u>?

	Adjuwant treatment	Risk of recurrence	
	Adjuvant treatment	Without treatment	With treatment
Dr Chaft	Chemotherapy → osimertinib	60%	30%
Dr Heymach	Chemotherapy → osimertinib	45%	12%
Dr Awad	Chemotherapy → osimertinib	40%	25%
Dr Forde	Chemotherapy → osimertinib	50%	15%
Dr Govindan	Chemotherapy → osimertinib	50%	30%
Dr Wakelee	Chemotherapy → osimertinib	70%	20%

Regulatory and reimbursement issues aside, in general, which adjuvant treatment would you recommend for an otherwise healthy 65-year-old patient with <u>Stage IIA</u> nonsquamous NSCLC and a <u>PD-L1 TPS of 50%</u>? What would you estimate to be the approximate risk of recurrence if the patient <u>did versus did not</u> receive adjuvant therapy?

	Adjuwant treatment	Risk of re	currence
	Adjuvant treatment	Without treatment	With treatment
Dr Chaft	Carboplatin-based chemotherapy → atezolizumab	45%	20%
Dr Heymach	Carboplatin-based chemotherapy → atezolizumab	45%	30%
Dr Awad	Cisplatin-based chemotherapy → pembrolizumab	35%	20%
Dr Forde	Cisplatin-based chemotherapy → atezolizumab	40%	10%-15%
Dr Govindan	Cisplatin-based chemotherapy → atezolizumab	30%	25%
Dr Wakelee	Cisplatin-based chemotherapy → atezolizumab	70%	25%

Regulatory and reimbursement issues aside, in general, which adjuvant treatment would you most likely recommend for an otherwise healthy 65-year-old patient with completely resected <u>Stage IIB</u> adenocarcinoma of the lung and a <u>PD-L1 TPS of 50%</u>? What would you estimate to be the approximate risk of recurrence if the patient <u>did versus did not receive adjuvant therapy</u>?

	Adjuvant treatment	Risk of recurrence	
	Adjuvant treatment	Without treatment	With treatment
Dr Chaft	Cisplatin-based chemotherapy → atezolizumab	60%	30%
Dr Heymach	Carboplatin-based chemotherapy → atezolizumab	60%	25%
Dr Awad	Cisplatin-based chemotherapy → pembrolizumab	40%	25%
Dr Forde	Cisplatin-based chemotherapy → atezolizumab	50%	25%
Dr Govindan	Cisplatin-based chemotherapy → pembrolizumab	50%	30%
Dr Wakelee	Cisplatin-based chemotherapy → atezolizumab	70%	30%-35%

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Case Presentation – Dr Heymach: targeted therapy

- 51-year-old non-smoker, mother of 5, found to have LUL mass in 2021
 - PS 0, exercises diligently, highly active and motivated.
- After resection found to have stage II lung adeno (T2N1M0), PD-L1<1%.
- On sequencing found to have RET fusion.



Making Cancer History

Case Presentation – Dr Heymach: targeted therapy (continued)

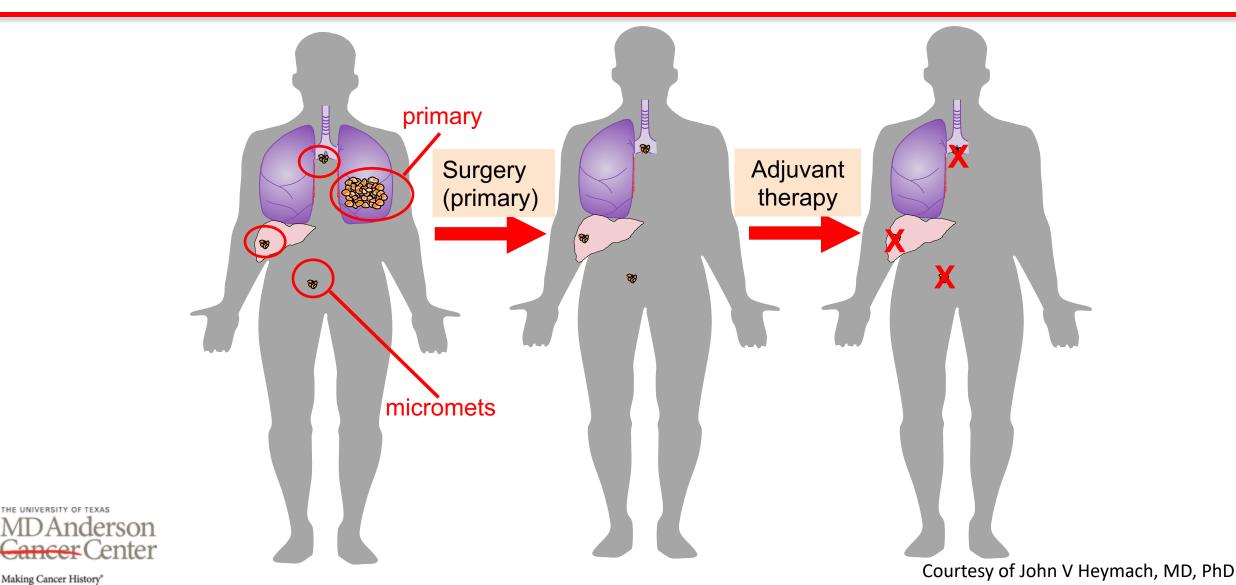
- Patient requests adjuvant selpercatinib but SOC is discussed with patient, chemo is offered.
- Patient reluctantly completes 4 cycles of cis/pemetrexed uneventfully.
- She requests ctDNA monitoring.
- After 1-year ctDNA is positive and solitary liver metastasis observed.
- Liver met resected and (sort of) adjuvant selpercatinib started.
- Patient remains recurrence free July 2023.



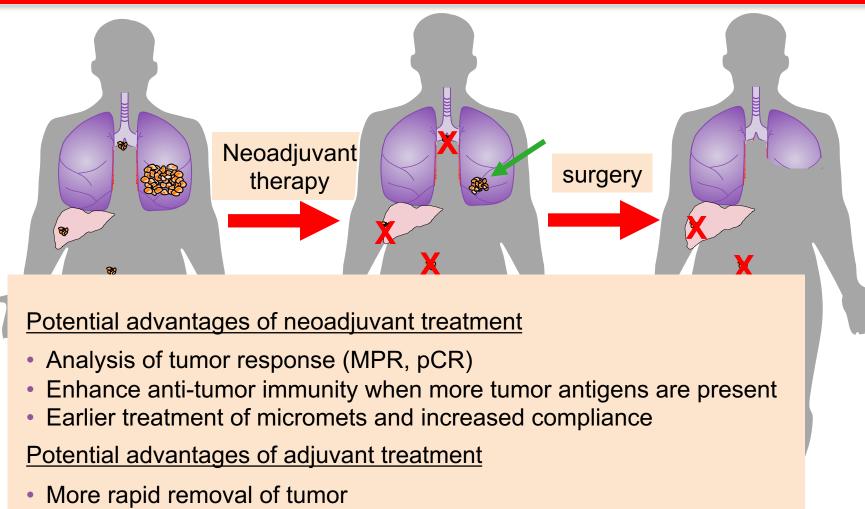
Have you recommended or would you recommend targeted therapy in the adjuvant setting for a patient with NSCLC and ...?

	An EGFR mutation	An ALK rearrangement	A RET rearrangement
Dr Chaft	Yes	Yes	No
Dr Heymach	Yes	Yes	Yes
Dr Awad	Yes	Yes	No
Dr Forde	Yes	Yes	No
Dr Govindan	Yes	Νο	Νο
Dr Wakelee	Yes	Yes	No

The primary goal of adjuvant treatment is to eliminate micrometastatic disease



Neoadjuvant treatment can "downstage" the primary tumor, potentially making surgery less morbid and clearing mediatinum



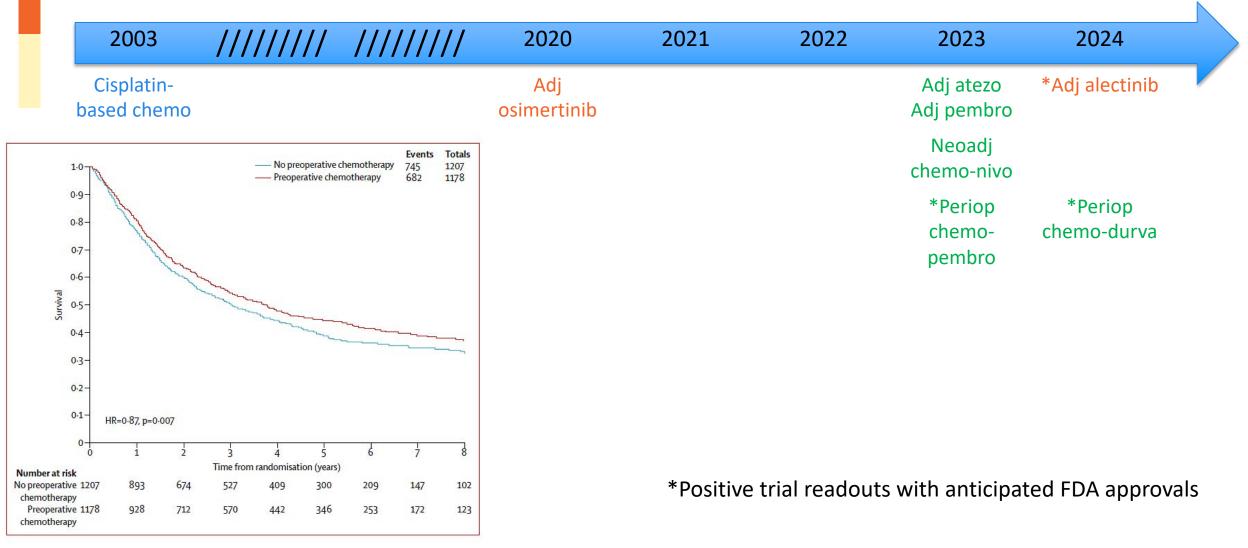
• No need for profiling prior to surgery

Courtesy of John V Heymach, MD, PhD



Making Cancer History'

Overview



Neoadj therapy meta-analysis equivalent HR to adjuvant therapy 0.87

Courtesy of Jamie E Chaft, MD



ADAURA study design: Adjuvant osimertinib for resectable EGFR mutant NSCLC

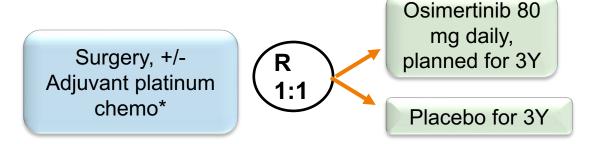


Key eligibility

- Stage IB-IIIA
- EGFRm (Ex19del, L858R)
- Complete resection with negative margins
- Max. interval between surgery and randomization: 10weeks (w/o adjuvant), 26w (w/adjuvant)

Stratification:

- Stage (IB vs II vs IIIA)
- EGFRm (Ex19del vs L858R)
- race (Asian vs non-Asian)



<u>Primary endpoint</u>: DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70

<u>Secondary endpoints include</u>: OS; DFS in the overall population; DFS at 2, 3, 4, and 5 years; safety, health-related QOL

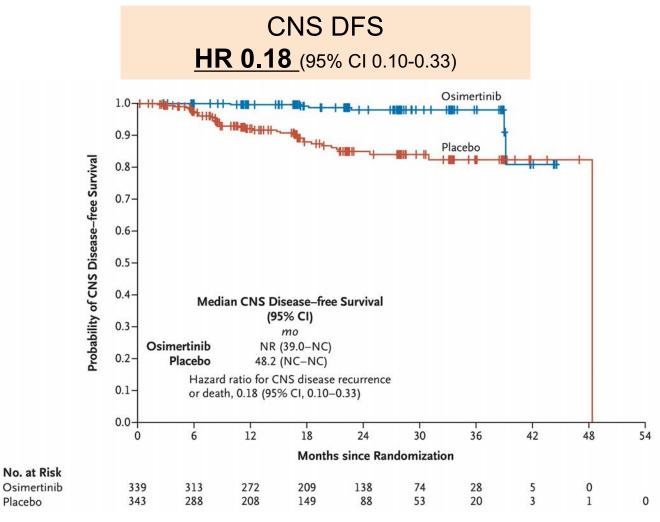
Courtesy of John V Heymach, MD, PhD



THE UNIVERSITY OF TEXAS

Making Cancer History*

ADAURA: Adjuvant osimertinib for resectable EGFR mutant NSCLC – CNS DFS



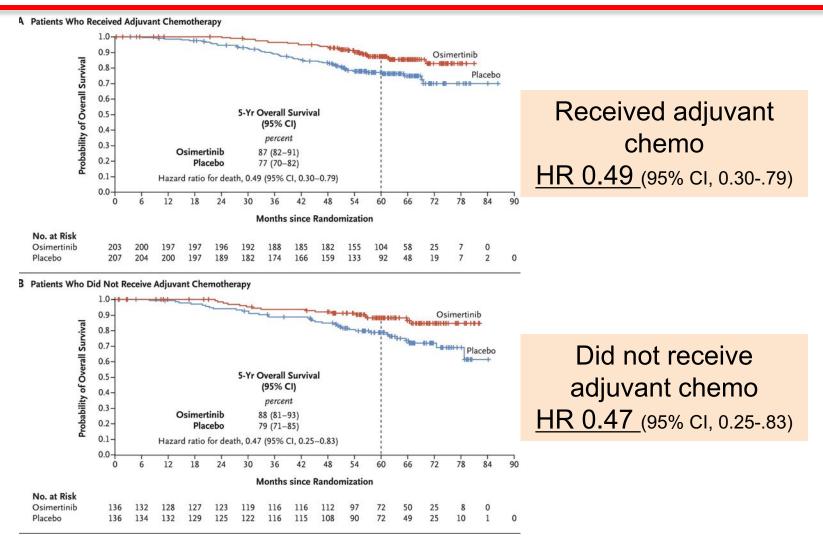


Making Cancer History*

Wu Y-L et al. N Engl J Med 2020;383:1711-1723

Courtesy of John V Heymach, MD, PhD

ADAURA: OS benefit among those who did or did not receive adjuvant chemotherapy



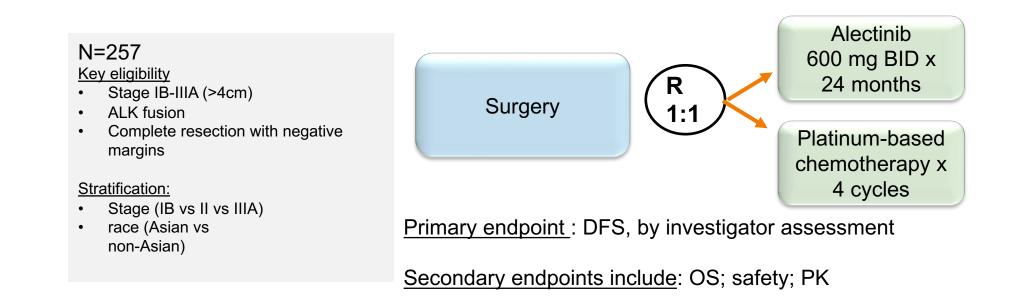


Making Cancer History'

Tsuboi M et al. N Engl J Med 2023;389:137-147

Courtesy of John V Heymach, MD, PhD

ALINA study design: Adjuvant alectinib for resectable ALK mutant NSCLC



Press release Sept. 1, 2023: Alectinib met its primary endpoint at prespecified interim analysis with a "statistically significant and clinically meaningful improvement in DFS as adjuvant therapy "



Making Cancer History*

Solomon et al, Proc ASCO 2019

Courtesy of John V Heymach, MD, PhD

What do you predict will be the hazard ratio for disease-free survival in the Phase III ALINA study evaluating alectinib versus platinum chemotherapy for patients with completely resected Stage IB to IIIA NSCLC and ALK alterations?

Dr Chaft	0.2
Dr Heymach	0.15 – 0.2
Dr Awad	0.3
Dr Forde	0.18
Dr Govindan	0.4
Dr Wakelee	0.2



Adjuvant therapy for resectable NSCLC: the bottom line

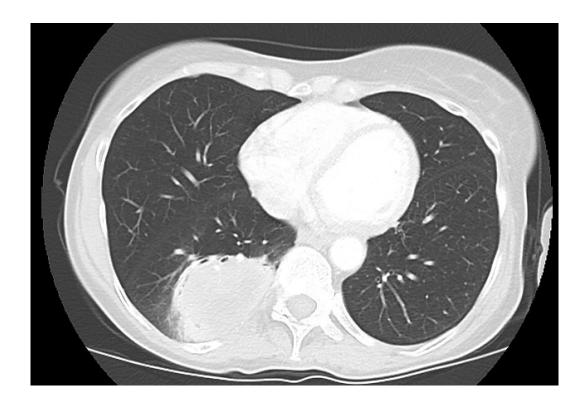
Targeted therapy

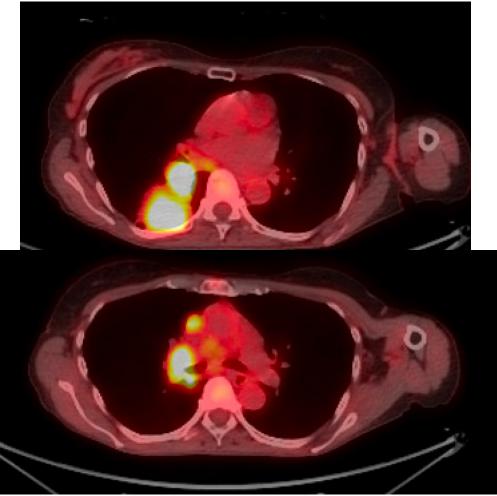
- ADAURA: Adjuvant Osimertinib x 3y improves DFS and OS
- ALINA: Alectinib improves DFS in ALK+ (press release)
- All resectable patients need profiling (EGFR/ALK minimum)



Case Presentation – Dr Chaft: osimertinib

- 6o-year-old female never smoker with a cT₃N₂ (hilar and level 7+) adenocarcinoma
- EGFR Exon 19 indel

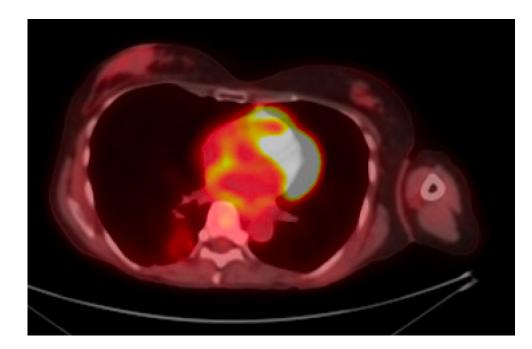


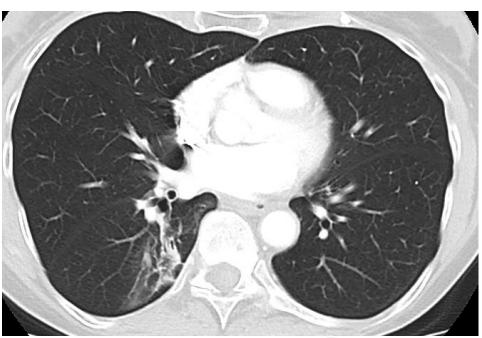




Case #3 T3N2

- Declined study (requires core bx)
- Refused chemo
- Treated with osi with near CR







Case #3 Path

- Went outside for resection frozen section level 3+ so surgeon wedged out primary and sampled a few nodes but didn't complete dissection. ypT1aNo
- Returned to us restaging with some mild adenopathy
- Complete resection done
 - No residual viable nodal disease
- Intolerant of adj chemo
- Resumed osi





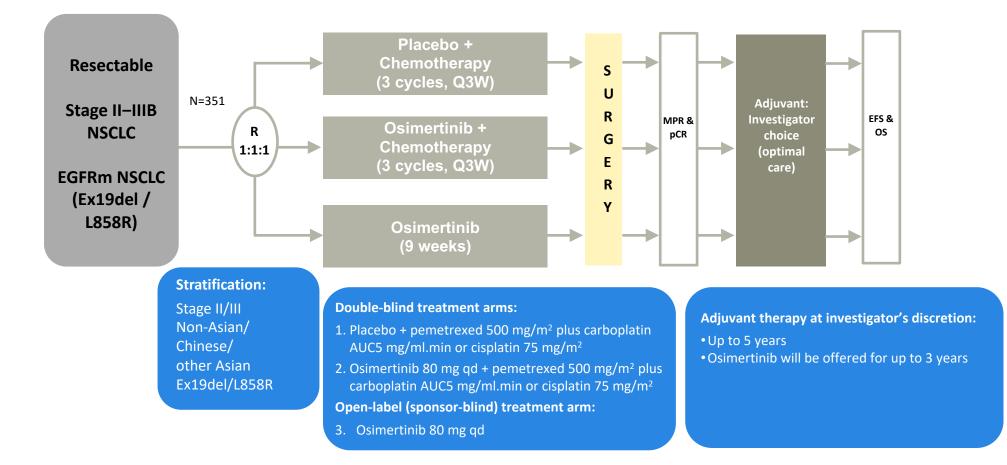
Neoadjuvant TKI

- Rationale is great, however very small datasets available
- Most data show failure to achieve high pCR rate
- Post-op chemo often poorly tolerated
- What about combination therapy?



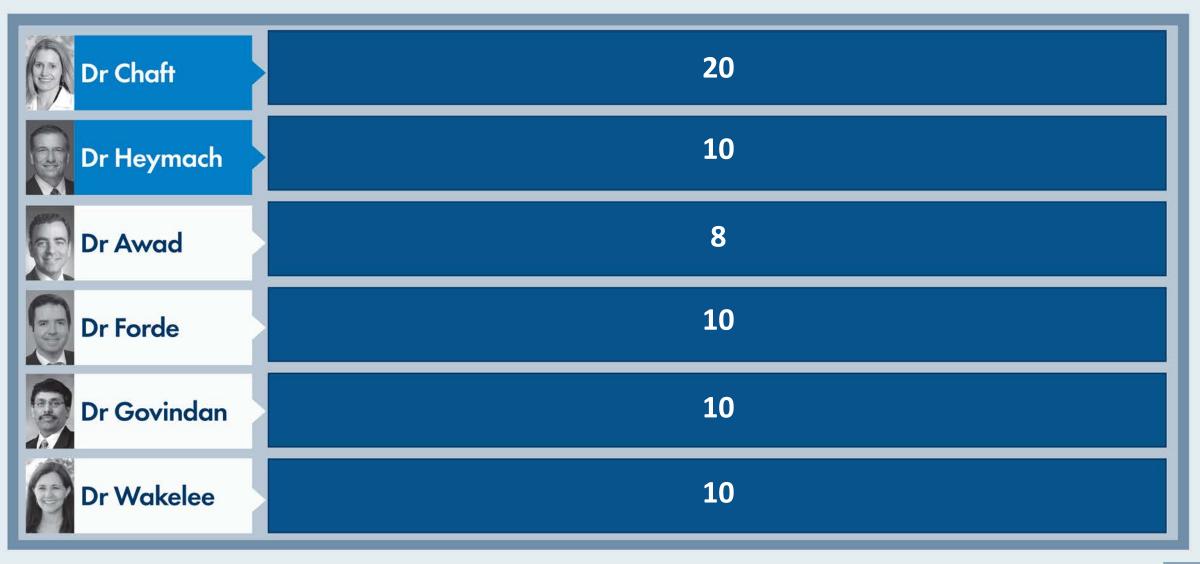
NeoADAURA (NCT 04351555)

Phase III, Randomized, Controlled, Multicenter Study of Neoadjuvant Osimertinib





To approximately how many patients with localized NSCLC have you administered adjuvant osimertinib?





Approximately what proportion of patients with localized NSCLC will experience toxicity during treatment with osimertinib that requires dosing to be held? What is the primary toxicity patients experience that leads to withholding dosing?

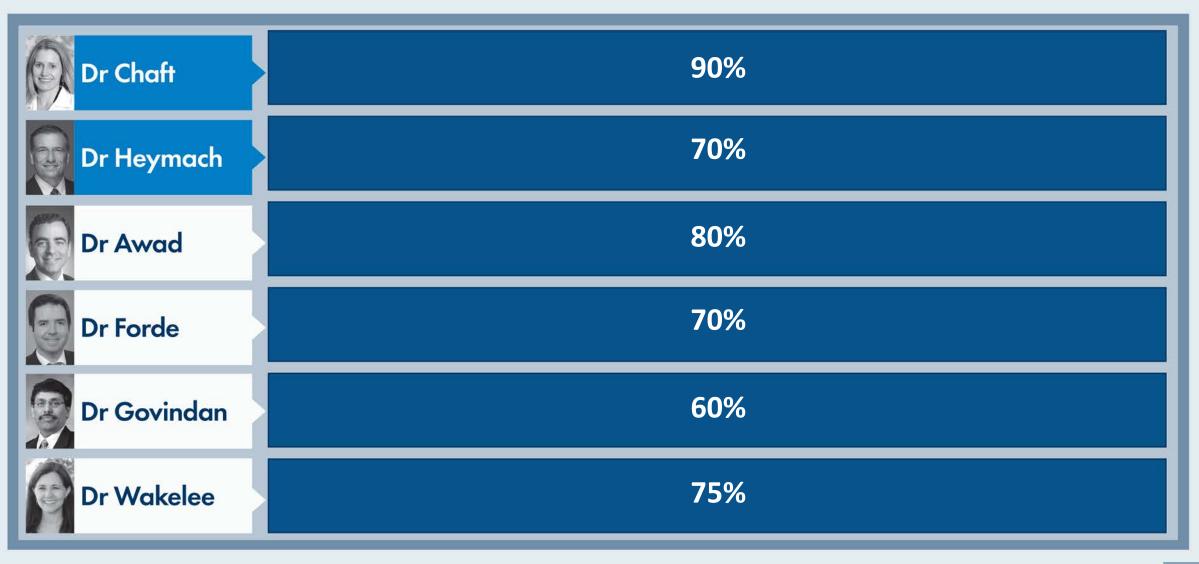
	Chance of holding dose	Primary toxicity	
Dr Chaft	5%	Pulmonary	
Dr Heymach	20%	Diarrhea	
Dr Awad	15%	GI toxicity	
Dr Forde	30%	Skin	
Dr Govindan	30%	Diarrhea, fatigue	
Dr Wakelee	5%	Pulmonary	

For how long do you typically continue adjuvant osimertinib for a patient with localized NSCLC who is tolerating therapy well? What variables, if any, affect your decision about duration of therapy?

Dr Chaft	Indefinitely for Stage III, 3-5 years for Stage II	
Dr Heymach	3 years	
Dr Awad	3 years, starting to discuss indefinite treatment if patients are tolerating treatment well	
Dr Forde	Indefinitely, will discuss at 3 years	
Dr Govindan	3 years	
Dr Wakelee	Discuss indefinite treatment	



Approximately what proportion of patients do you expect to complete your intended duration of adjuvant osimertinib?





To what degree do you believe adherence is an issue among patients receiving adjuvant osimertinib for localized NSCLC?





Do you generally hold adjuvant osimertinib for patients undergoing surgical procedures?

Dr Chaft	No	
Dr Heymach	Yes, starting day before and continuing for 3-4 days after	
Dr Awad	Yes, for about a week before/after major surgery	
Dr Forde	Yes, if any history of thrombocytopenia on receiving osimertinib will hold if surgeon prefers	
Dr Govindan	No	
Dr Wakelee	No	

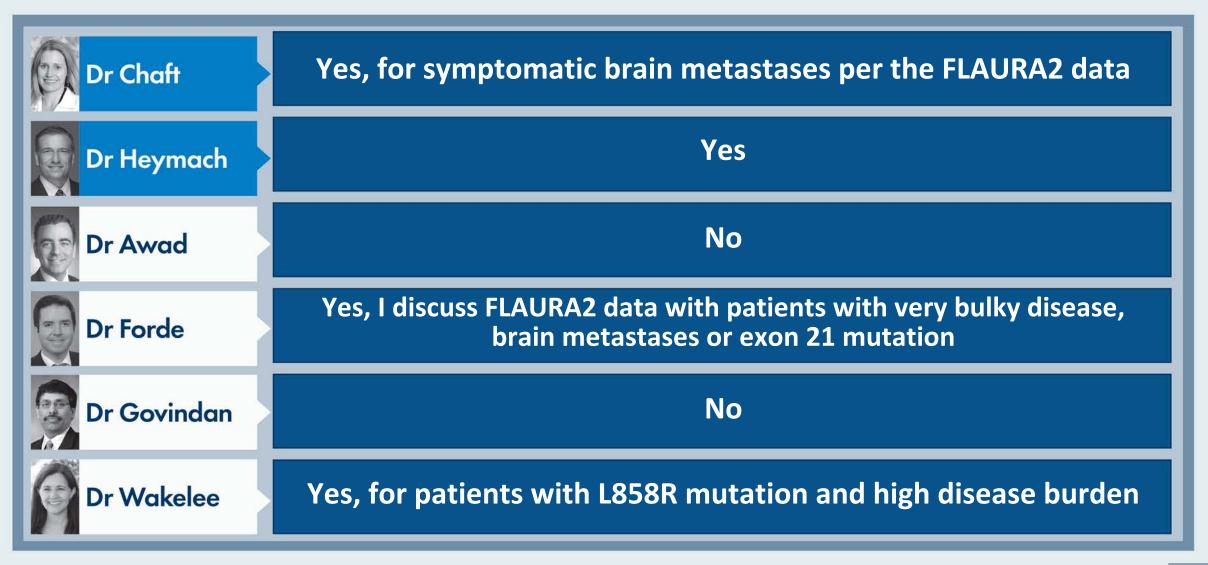


For a patient with an EGFR mutation who does not wish to receive chemotherapy, in which situations, if any, would you be comfortable administering adjuvant osimertinib alone?

Dr Chaft	I feel comfortable administering adjuvant osimertinib in all situations if a patient refuses chemotherapy	
Dr Heymach	Particularly for older patients or patients with renal issues	
Dr Awad	All situations (about one third of patients on ADAURA didn't get chemo)	
Dr Forde	Patients are informed of the survival benefit with chemotherapy; if they wish to proceed without it then will prescribe osimertinib alone	
Dr Govindan	I feel comfortable administering adjuvant osimertinib in all situations if a patient refuses chemotherapy	
Dr Wakelee	In most situations, but would discuss chemo for Stage III especially	



Is there a clinical scenario in which you would use chemotherapy with osimertinib as first-line treatment for a patient with metastatic NSCLC with an EGFR mutation?





Which of the following best describes your reaction to the recently reported final overall survival analysis of the Phase III ADAURA trial evaluating adjuvant osimertinib for patients with completely resected Stage IB to IIIA NSCLC with EGFR mutations?

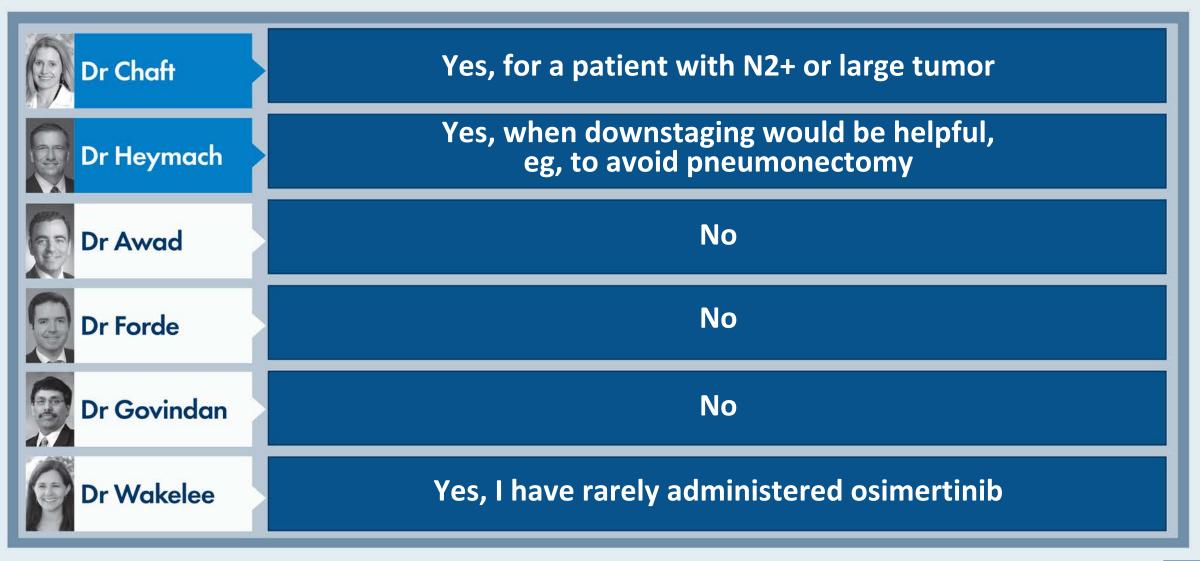
Dr Chaft	Results were similar to what I expected	
Dr Heymach	Results were slightly more positive than I expected	
Dr Awad	Results were slightly more positive than I expected	
Dr Forde	Results were much more positive than I expected	
Dr Govindan	Results were similar to what I expected	
Dr Wakelee	Results were slightly more positive than I expected	



Regulatory and reimbursement issues aside, what would you most likely recommend as consolidation treatment for a patient with locally advanced NSCLC who has completed chemoradiation therapy and is found to have ...?

	An EGFR-activating mutation	A RET fusion	
Dr Chaft	Osimertinib	2 cycles of chemotherapy	
Dr Heymach	Osimertinib	Selpercatinib	
Dr Awad	Osimertinib	Durvalumab	
Dr Forde	Osimertinib	Durvalumab	
Dr Govindan	Durvalumab	Durvalumab	
Dr Wakelee	Osimertinib	Additional pemetrexed	

Outside of a clinical trial setting, would you employ neoadjuvant targeted therapy for a patient with NSCLC and a documented genomic alteration (eg, EGFR mutation)?





Agenda

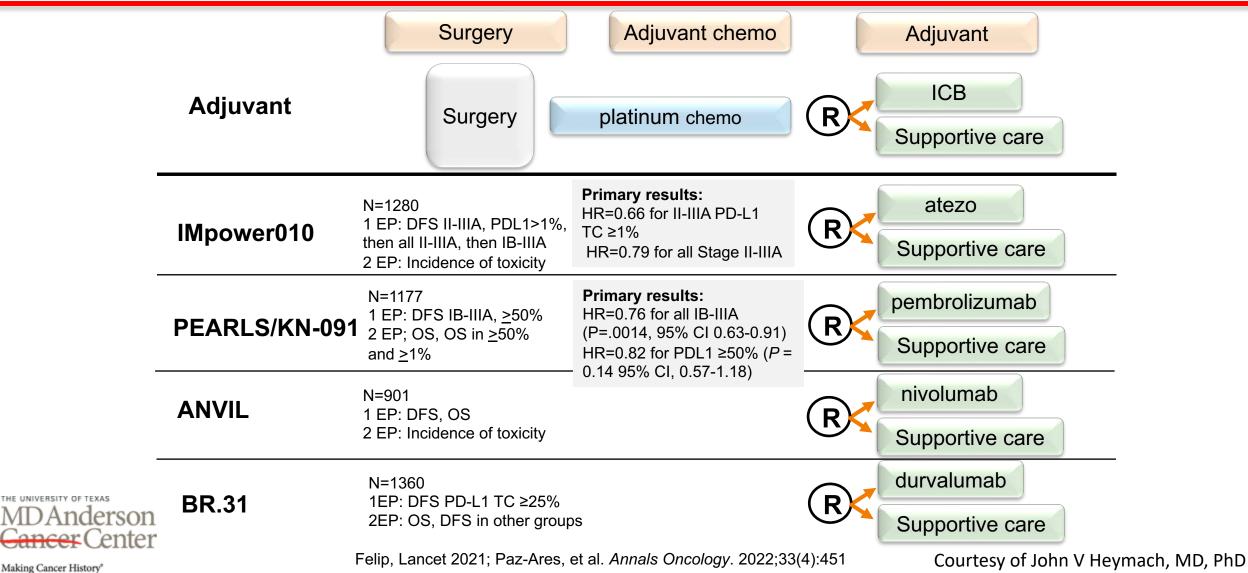
INTRODUCTION: Patient Involvement in (Neo)Adjuvant Treatment Decisions

MODULE 1: Targetable Treatment in Localized Disease

MODULE 2: Immunotherapy in Localized Disease



Randomized studies of adjuvant ICB for resectable NSCLC



What about IO after definitive RT? The I-SABR RP2 study for early-stage or isolated lung parenchymal recurrent node-negative NSCLC

N=156 randomized Key eligibility Stage IA-IIB, AJCC 8th ed. Or isolated parenchymal recurrence (node-SABR negative) Surgery, +/-R Medically inoperable or refused Adjuvant platinum 1:1 surgery chemo* SABR + nivolumab Stratification: 480mg Qw4 x 4 ECOG PS (0–1 vs 2), tumor size (\leq 3 cycles starting d1 of cm vs >3 to 5 cm vs >5 to 7 cm), RT histology (squamous vs nonsquamous), and lung cancer history (primary vs recurrent disease)

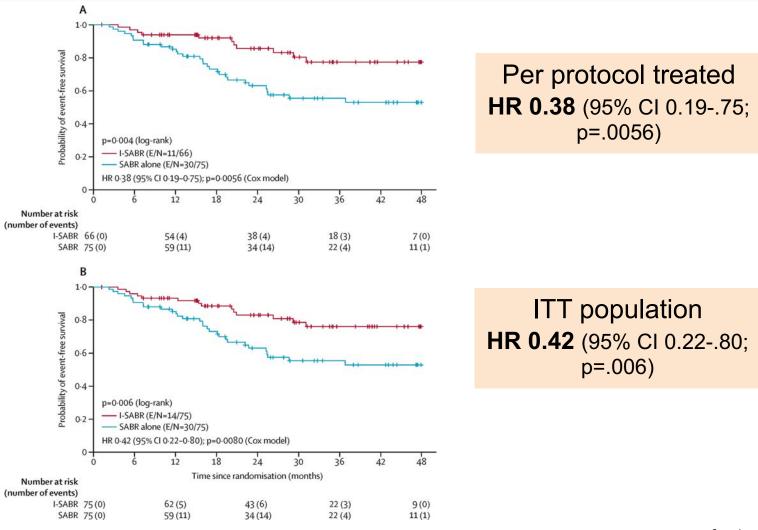
<u>Primary endpoint :</u> 4Y EFS (events include recurrence, new primary, or death), both ITT and treatment per-protocol



Chang et al, Lancet 2023

Making Cancer History*

I-SABR RP2 study for early-stage or isolated lung parenchymal recurrent node-negative NSCLC: primary results





Making Cancer History'

Chang et al, Lancet 2023

Courtesy of John Heymach MD, PhD

Adjuvant therapy for resectable NSCLC: the bottom line

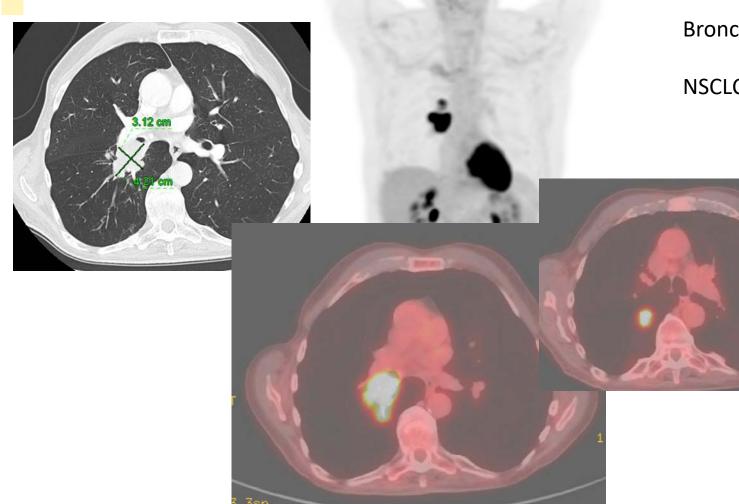
<u>ICB</u>

- Adjuvant ICB improves outcomes in resectable NSCLC in overall population although benefit generally greater in higher PD-L1 levels
- Pembro approved stages IB-IIIA (any PD-L1), atezo in PD-L1 >1%
- Initial results suggest adjuvant nivolumab improves EFS after SABR



Case Presentation – Dr Chaft: cT2aN1, Stage IIB

70-year-old male former smoker presents with cough



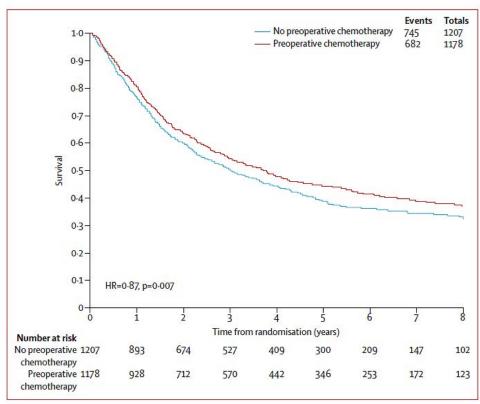
Bronch bx: (primary tumor, LN not accessible):

NSCLC, favor squamous cell, PD-L1 60%



Why Induction?

- Regression from the hilum may enable lesser resection
- Prehabilitation
- In vivo treatment efficacy assessment



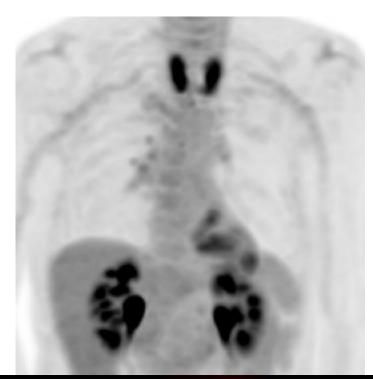


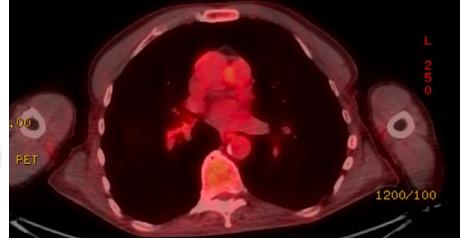
Post-treatment evaluation

- CT PR after 2 cycles
- Scintigraphic PR
- Notably thyroiditis
- Severe hypothyroidism on labs
- No Al

How do I follow these folks?

CT Chest w/con after 2 cycles PET/MR brain with endo labs (on the day of scans, so results in your hand when pt returns) after 3rd cycle







Courtesy of Jamie E Chaft, MD

Case #1 Summary

- Nice radiographic response to chemo-IO
- Surgery delayed to manage IO induced hypothyroidism
 - Induction of anesthesia when severely hypothyroid can lead to vascular collapse
- Pt went to the OR last week, path report pending
- He will need continued endo lab follow-up



Case #1 Outcomes to query

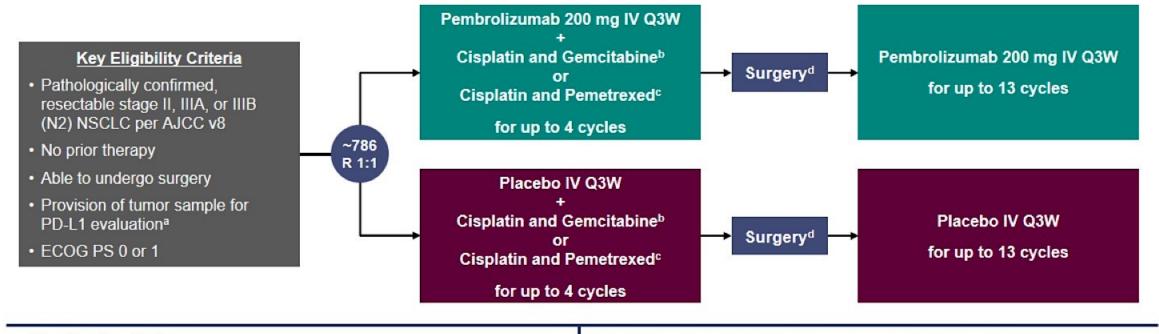
CM-816 didn't prespecify adjuvant therapy

- What if he has a pCR, any more therapy needed?
- What if he doesn't have a pCR?
- Who is going to follow his endocrinopathies?
- When is he safely out of the window of developing a new IRAE?

I will watch... if carbo/pacli/nivo didn't do the trick, gem monotherapy or more IO play no role without more data



KEYNOTE-671 Study Design Randomized, Double-Blind, Phase 3 Trial



Stratification Factors

- Disease stage (II vs III)
- PD-L1 TPS^a (<50% vs ≥50%)

#ASCO23

- Histology (squamous vs nonsquamous)
- · Geographic region (east Asia vs not east Asia)

Dual primary end points: EFS per investigator review and OS

Key secondary end points: mPR and pCR per blinded, independent pathology review, and safety

^a Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. ^b Cisplatin 75 mg/m² IV Q3W + gemcitabine 1000 mg/m² IV on days 1 and 8 Q3W was permitted for squamous histology only. ^c Cisplatin 75 mg/m² IV Q3W + pemetrexed 500 mg/m² IV Q3W was permitted for nonsquamous histology only. ^d Radiotherapy was to be administered to participants with microscopic positive margins, gross residual disease, or extracapsular nodal extension following surgery and to participants who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.





Wakelee KN671 ASCO 2023

KEYNOTE-671: Event-Free Survival

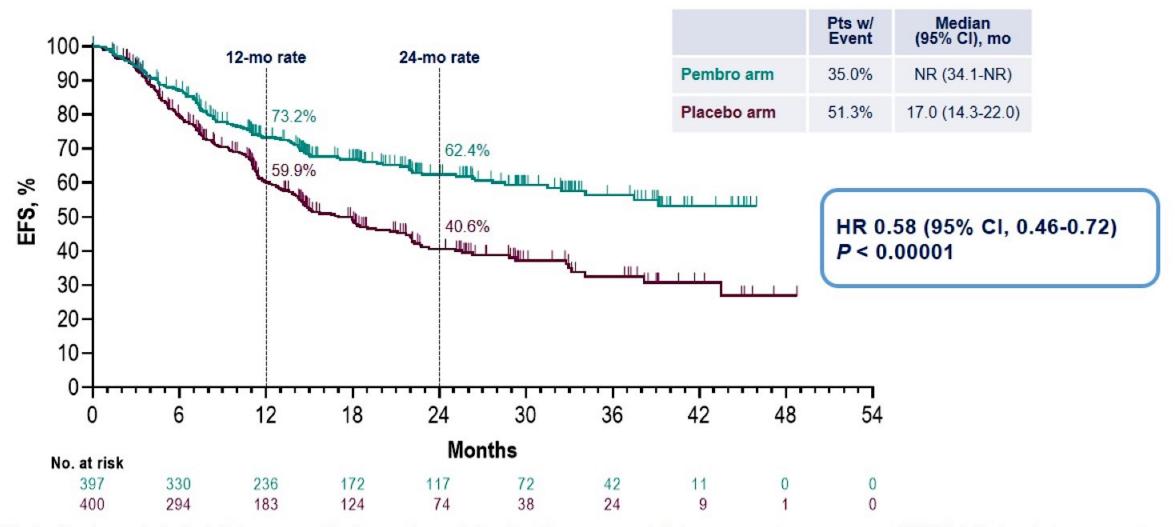
PRESENTED BY: Dr. Heather Wakelee

2023 ASCO

ANNUAL MEETING

#ASCO23

N Engl J Med 2023 Aug 10;389(6):491-503.

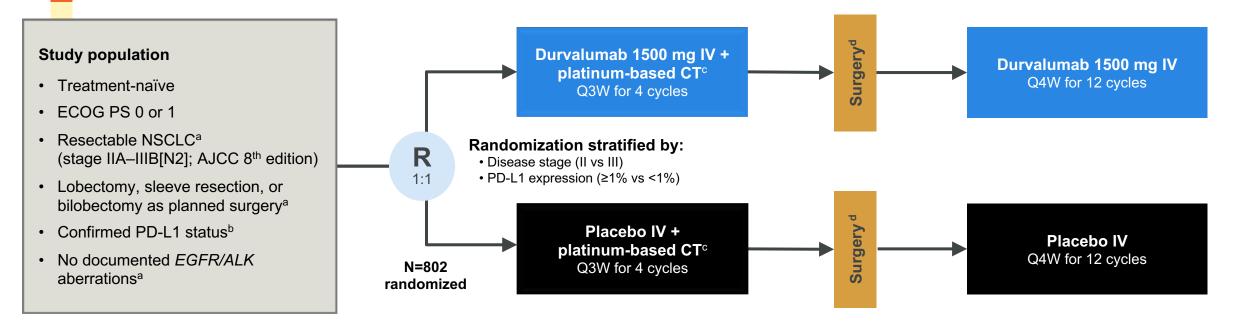


EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).



Courtesy of Jamie E Chaft, MD

AEGEAN: Study Design



Endpoints: All efficacy analyses performed on a modified population that excludes patients with documented EGFR/ALK aberrations^e

Primary:

- pCR by central lab (per IASLC 2020)
- EFS using BICR (per RECIST v1.1)

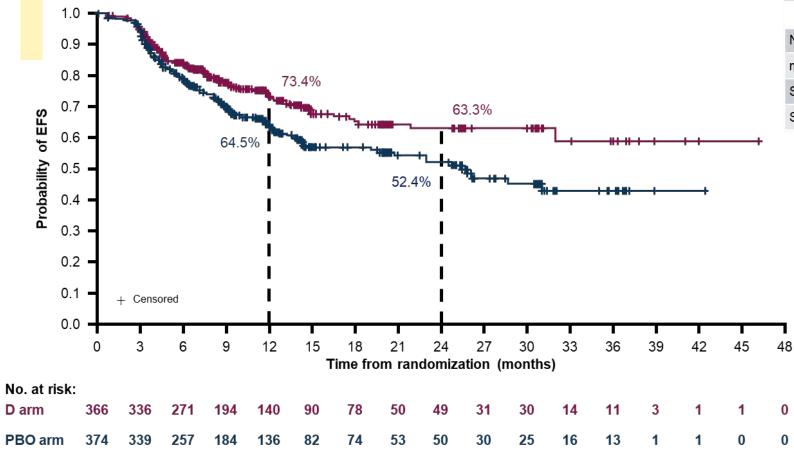
Key secondary:

- MPR by central lab (per IASLC 2020)
- DFS using BICR (per RECIST v1.1)
- OS

Courtesy of Jamie E Chaft, MD



AEGEAN: EFS



	D arm	P arm
No. events / no. patients (%)	98/366 (26.8)	138/374 (36.9)
mEFS, months (95% CI)	NR (31.9–NR)	25.9 (18.9-NR)
Stratified HR* (95% CI)	0.68 (0.5	53–0.88)
Stratified log-rank P-value	0.003902	

Median follow-up (range) in censored patients: 11.7 months (0.0-46.1)

EFS maturity: 31.9%



Take home messages on Neoadjuvant Therapy

- Induction IO likely more effective than adjuvant IO
- Predictive biomarker testing remains important – not IO for all
- Personalized medicine needs to be employed in the perioperative setting too
 - Disease characteristics (location, hemoptysis, obstruction)
 - Tumor biology (PD-L1 genomics)
 - Pt characteristics (comorbidities)
 - Pt preference (without comparative data between pre/postop)



In which specific clinical situations do you or would you administer adjuvant chemotherapy followed by an anti-PD-1/PD-L1 antibody?

Dr Chaft	Stage II/III resected, PD-L1-positive, EGFR/ALK/ROS/RET/HER2-negative
Dr Heymach	Only if resected prior to seeing me, or unwilling to wait for neoadjuvant; otherwise, I prefer neoadjuvant
Dr Awad	In a situation such as this: Some surgeons take patients straight to surgery without discussing neoadjuvant therapy, or they discover that the pathologic stage is actually II (eg, was clinical Stage I going into surgery)
Dr Forde	Upstaged from clinical Stage I to higher pathologic stage at surgery, candidate for adj chemo; I tend to recommend adj IO only for patients with PD-L1 ≥50% but discuss and have used with 1%-49%
Dr Govindan	All patients with NSCLC who would be candidates for lobectomy
Dr Wakelee	Select resected Stage II, and all resected Stage III especially with high PD-L1; but not to patients with a driver mutation that is nonresponsive to IO



Think of the last patient to whom you administered adjuvant chemotherapy followed by an anti-PD-1/PD-L1 antibody. What was their ...?

	Age	Sex	Disease stage	PD-L1 status
Dr Chaft	65	Female	IIB	50%
Dr Heymach	67	Male	IIB	50%
Dr Awad	66	Female	IIB	1%
Dr Forde	52	Female	IIIA	30%
Dr Govindan	67	Male	II	Positive
Dr Wakelee	73	Male	II	30%

Do you have a preferred choice of agent when recommending adjuvant immunotherapy for a patient with localized NSCLC?

Dr Chaft	Yes, atezolizumab	
Dr Heymach	Yes, atezolizumab for PD-L1-positive, pembrolizumab for PD-L1-negative	
Dr Awad	Yes, pembrolizumab	
Dr Forde	Yes, atezolizumab	
Dr Govindan	No preference	
Dr Wakelee	Yes, atezolizumab	



Does PD-L1 level affect your preference of adjuvant immunotherapy for localized NSCLC?

Dr Chaft	Yes, PD-L1 high: atezolizumab, PD-L1 low: either, PD-L1-negative: pembrolizumab
Dr Heymach	Yes, atezolizumab for PD-L1-positive, pembrolizumab for PD-L1-negative
Dr Awad	Yes, more likely to omit it if PD-L1-negative if there may be a contraindication (eg, history of autoimmune disease)
Dr Forde	Yes, the consistency of the atezolizumab data across PD-L1 strata is reassuring and I tend to favor it
Dr Govindan	No
Dr Wakelee	Yes, atezolizumab if PD-L1 high, and I question the benefit of adjuvant IO in those with negative PD-L1

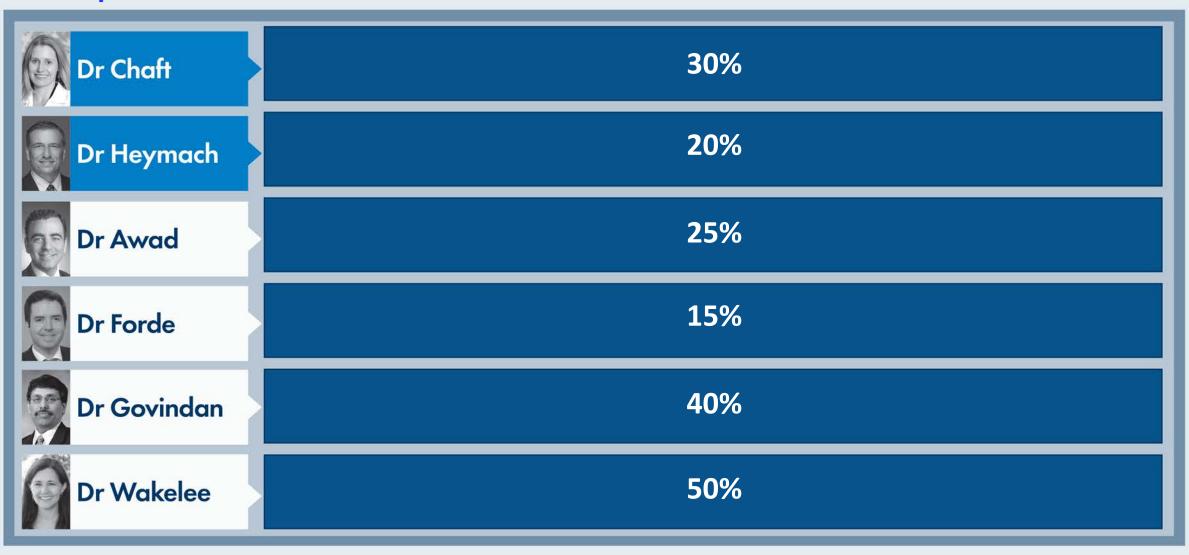


For a patient who does not wish to receive chemotherapy, in which situations, if any, would you be comfortable administering an adjuvant anti-PD-1/PD-L1 antibody alone?

Dr Chaft	PD-L1 high or PD-L1 low and smoker or TMB high	
Dr Heymach	PD-L1-positive	
Dr Awad	I would still explain the benefit of chemotherapy, but if they do not want it, I would use adjuvant IO alone for Stage II/III, regardless of PD-L1 level	
Dr Forde	I am hesitant to recommend adjuvant IO alone but will consider if the pt is insistent they will not take chemo and the tumor is PD-L1 positive, ideally 50%+	
Dr Govindan	Smokers with PD-L1 of 50% or greater	
Dr Wakelee	No positive data with this; I'd be very hesitant but would discuss with a patient with very high tumor PD-L1 (no driver mutation) who absolutely refused chemo	

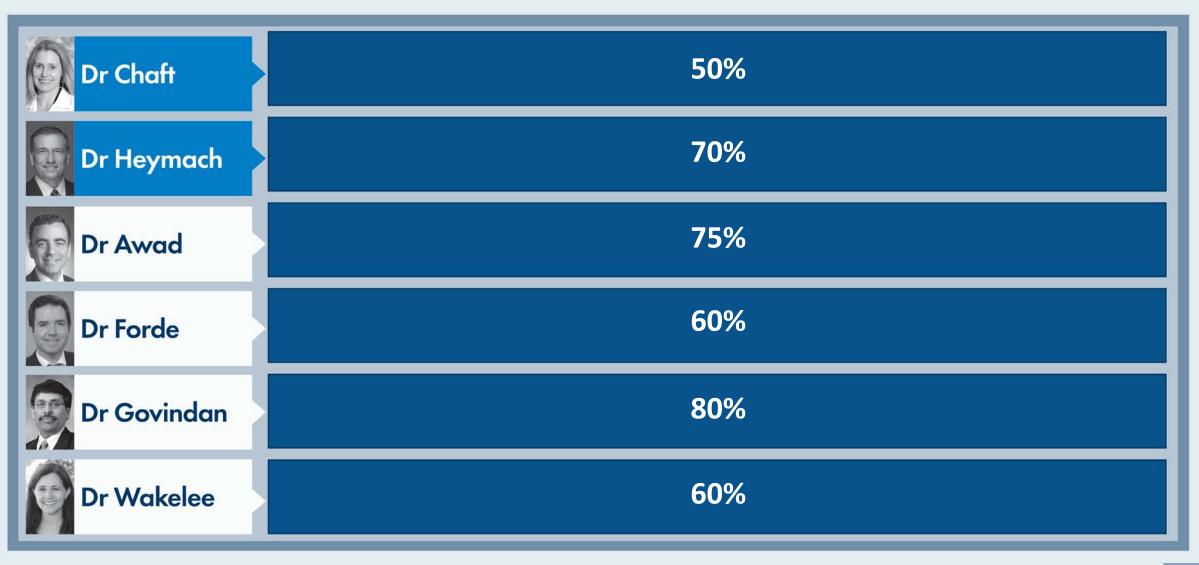


Based on your clinical experience and knowledge of available data, what would you estimate is the likelihood that a patient receiving 1 year of adjuvant immunotherapy will experience an immune-related adverse event?





Approximately what proportion of patients receiving adjuvant immunotherapy for localized NSCLC complete treatment?



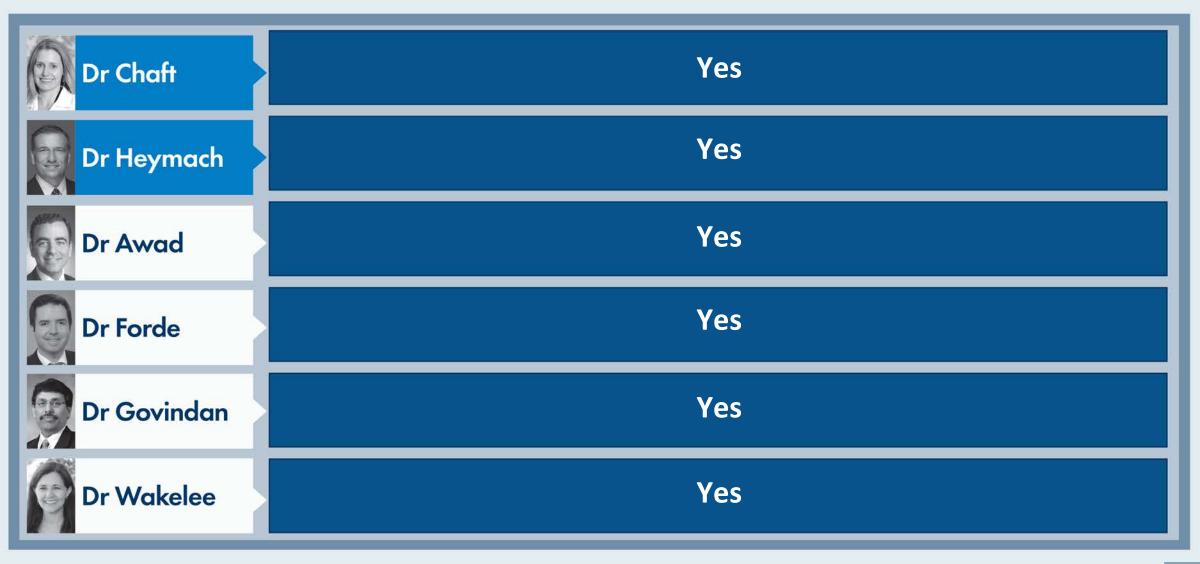


Based on your clinical experience and knowledge of available data, what are the top 3 side-effect issues patients experience when receiving adjuvant immunotherapy for localized NSCLC?

Dr Chaft	Pruritus/rash, hypothyroidism, arthralgias
Dr Heymach	Thyroiditis, pneumonitis, colitis
Dr Awad	Arthralgias, fatigue, hypothyroidism
Dr Forde	GI upset, thyroid function abnormalities, skin rash
Dr Govindan	Thyroid dysfunction, rash, asymptomatic pneumonitis
Dr Wakelee	Thyroid dysfunction, rash, arthralgias



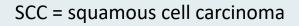
Do you believe that a correlation exists between autoimmune toxicity and treatment benefit among patients receiving immune checkpoint inhibitors?





Please describe 3 situations in which you considered adjuvant immunotherapy for a patient with a potential contraindication (eg, prior autoimmune disease). What was the nature of the contraindication, what did you ultimately decide and how did the patient respond? Patient 1

Dr Chaft	Controlled Crohn's disease, resected Stage IIA SCC, PD-L1-negative received adjuvant carboplatin/paclitaxel, no IO
Dr Heymach	Minor skin autoimmune (psoriasis, inactive)
Dr Awad	Recently active ulcerative colitis, PD-L1-negative, decided not to use adjuvant IO; currently receiving just adjuvant chemotherapy
Dr Forde	History of Graves disease, discussed with endocrinologist and they felt reasonable to proceed, patient fared well and is without recurrence
Dr Govindan	Lupus, discussed adjuvant IO but ultimately the patient did not receive this treatment
Dr Wakelee	Mild rheumatoid arthritis, discussed and treated with adjuvant IO, patient fared okay





Please describe 3 situations in which you considered adjuvant immunotherapy for a patient with a potential contraindication (eg, prior autoimmune disease). What was the nature of the contraindication, what did you ultimately decide and how did the patient respond? Patient 2

Dr Chaft	Resected Stage IIIA KRAS G12C+/KEAP1-/STK11-, PD-L1 100% and concurrently resected thymoma received adjuvant cisplatin/pemetrexed, no IO
Dr Heymach	High risk for relapse with history of RA (but RA history was soft — may have been osteoarthritis)
Dr Awad	Interstitial lung disease, PD-L1-negative, just received chemotherapy. Possible disease recurrence
Dr Forde	Vague history of lupus, never treated, rheumatology consult felt it was not lupus and patient received adjuvant IO without issues
Dr Govindan	Organ transplant, discussed adjuvant immunotherapy but ultimately the patient did not receive this treatment
Dr Wakelee	History of inflammatory bowel disease, discussed but patient decided against treatment



Please describe 3 situations in which you considered adjuvant immunotherapy for a patient with a potential contraindication (eg, prior autoimmune disease). What was the nature of the contraindication, what did you ultimately decide and how did the patient respond? Patient 3

Dr Chaft	Resected Stage IIIA N1 KRAS G12C+ LCNEC, PD-L1 90%, RA on prednisone and biologics, received adjuvant carboplatin/paclitaxel and atezolizumab
Dr Heymach	History of possible Crohn's, inactive, patient really motivated for treatment
Dr Awad	Remote h/o Crohn's colitis, not recently active, PD-L1 TPS 60%, currently faring well on adjuvant pembrolizumab
Dr Forde	Resected Stage IIB NSCLC, PD-L1 80%; history of "uveitis" and on steroid eye drops for years. Referred to ophthalmology, diagnosis of Fuchs heterochromic uveitis (late sequala of childhood rubella), ruled not a contraindication to IO and patient received adjuvant IO without any issues
Dr Govindan	Multiple sclerosis with optic neuritis, discussed adjuvant immunotherapy but ultimately the patient did not receive this treatment
Dr Wakelee	Paraneoplastic polymyalgia rheumatica which drastically improved after resection of Stage IIB NSCLC. We felt risk of IO was very high for a flare of her PMR

LCNEC = large cell neuroendocrine carcinoma of the lung; RA = rheumatoid arthritis



In which specific clinical situations do you or would you administer neoadjuvant chemotherapy combined with an anti-PD-1/PD-L1 antibody?

Dr Chaft	Clinical Stage II/III, medically operable and technically resectable NSCLC without actionable oncogene driver mutation and without pre-existing autoimmune disease
Dr Heymach	All EGFR and ALK wild-type patients with tumors larger than 4 cm
Dr Awad	All patients with Stage II/III resectable NSCLC (EGFR/ALK negative) who are otherwise eligible for chemotherapy and immunotherapy
Dr Forde	ECOG PS 0-1, limited comorbidities, resectable clinical Stage II/IIIA NSCLC without an EGFR mutation or ALK alteration
Dr Govindan	Locally advanced node-positive NSCLC who would be candidates for lobectomy
Dr Wakelee	Stage III without driver mutation, many but not all Stage II



Think of the last patient to whom you administered neoadjuvant chemotherapy combined with an anti-PD-1/PD-L1 antibody. What was their ...?

	Age	Sex	Disease stage	PD-L1 status
Dr Chaft	65	Male	IIB	30%
Dr Heymach	69	Female	IIIA	20%
Dr Awad	72	Male	IIIA	40%
Dr Forde	81	Male	IIB	0%
Dr Govindan	45	Female	IIIA	Positive
Dr Wakelee	52	Male	IIIA	10%

In general, for a patient with localized non-small cell lung cancer (NSCLC) to whom you have made the decision to administer an anti-PD-1/PD-L1 antibody in the neoadjuvant setting, what do you consider to be the optimal approach?

Dr Chaft	Neoadjuvant chemotherapy/nivolumab \rightarrow resection
Dr Heymach	Neoadjuvant chemotherapy/pembrolizumab \rightarrow resection \rightarrow adjuvant pembrolizumab
Dr Awad	Neoadjuvant chemotherapy/nivolumab $ ightarrow$ resection
Dr Forde	Neoadjuvant chemotherapy/nivolumab \rightarrow resection
Dr Govindan	Neoadjuvant chemotherapy/nivolumab $ ightarrow$ resection
Dr Wakelee	Neoadjuvant chemotherapy/nivolumab $ ightarrow$ resection



Does PD-L1 level affect your preference of neoadjuvant immunotherapy for localized NSCLC?

Dr Chaft	Yes, but strictly to determine whether to administer; PD-L1 level does not affect my choice of agent
Dr Heymach	No
Dr Awad	Not exactly, though I am more optimistic for using chemoimmunotherapy for cancers that are PD-L1-positive
Dr Forde	Yes, benefit of (neo)adjuvant IO is likely greater for PD-L1-positive disease; I tend to favor neoadjuvant chemotherapy/nivolumab for PD-L1-negative as it is a shorter course of therapy
Dr Govindan	No
Dr Wakelee	Yes, the concurrent with chemo approach is favored for those with low or no PD-L1 expression in my opinion, so lean towards neoadjuvant



What Clinicians Want to Know About the Management of Relapsed/Refractory Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Tuesday, September 26, 2023 5:00 PM – 6:00 PM ET

Faculty Toby A Eyre, MBChB, DipMedEd, MRCP, MD Brad S Kahl, MD

> Moderator Neil Love, MD



Thank you for joining us!

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CME and MOC credit information will be emailed to each participant within 5 business days.

