Expert Second Opinion: The Emerging Role of Immunotherapy and Targeted Treatment in Localized Non-Small Cell Lung Cancer

A Live Webinar Held as a Satellite CME/MOC Symposium During the IASLC 2021 World Conference on Lung Cancer Worldwide Virtual Event

Sunday, September 12, 2021
11:15 PM – 12:15 AM ET

Faculty

Edward B Garon, MD, MS
Jarushka Naidoo, MB BCH, MHS
Harvey I Pass, MD
Heather Wakelee, MD

Moderator

Neil Love, MD

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Faculty

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Director, Thoracic Oncology Program
Director, Signal Transduction and Therapeutics Research Program
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Chief, Division of Oncology
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Adjunct Assistant Professor of Oncology
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Baltimore, Maryland

Moderator
Neil Love, MD
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Miami, Florida

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Commercial Support

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Dr Pass — Disclosures

No relevant conflicts of interest to disclose

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Dr Wakelee — Disclosures

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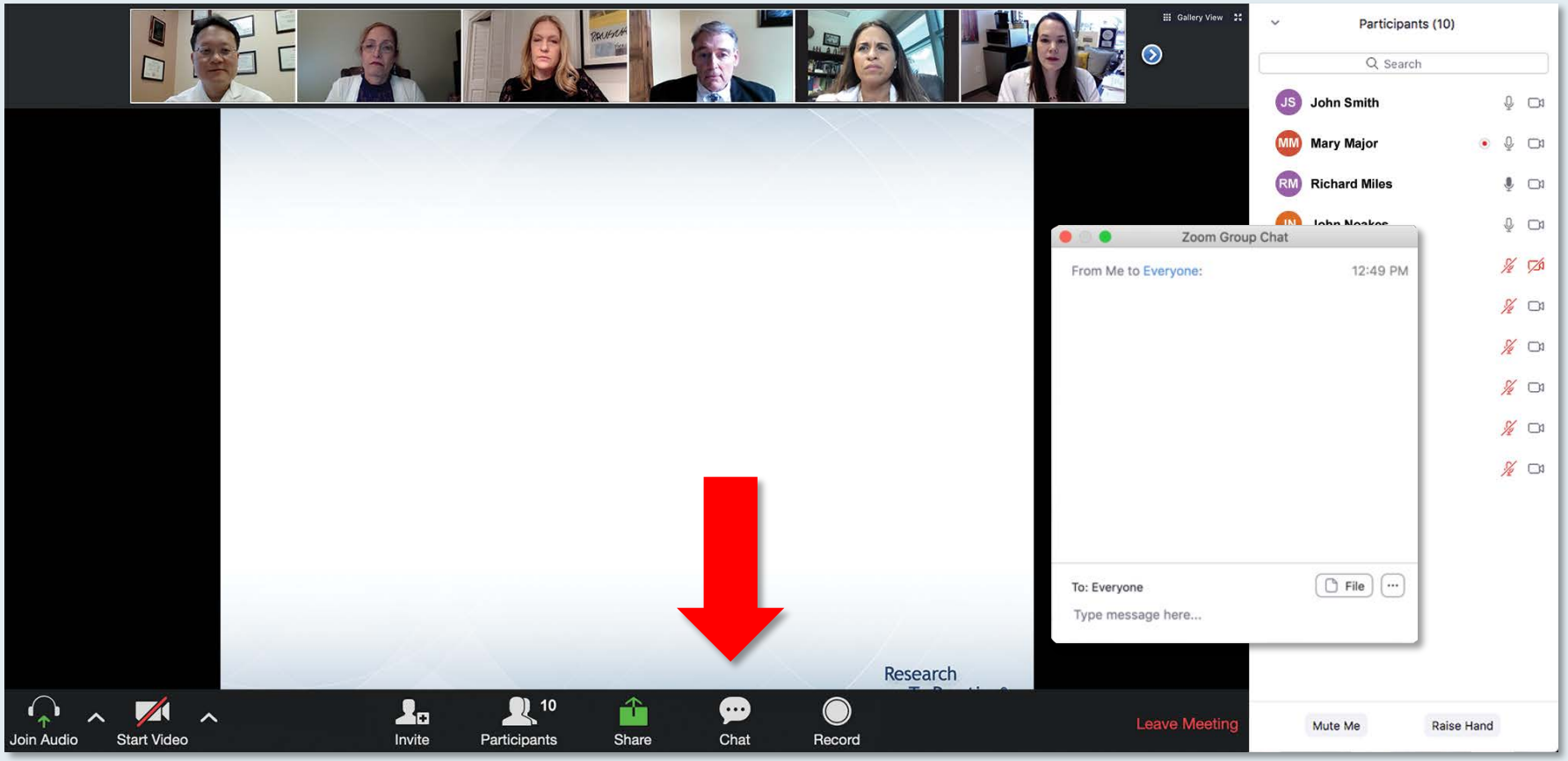
We Encourage Clinicians in Practice to Submit Questions



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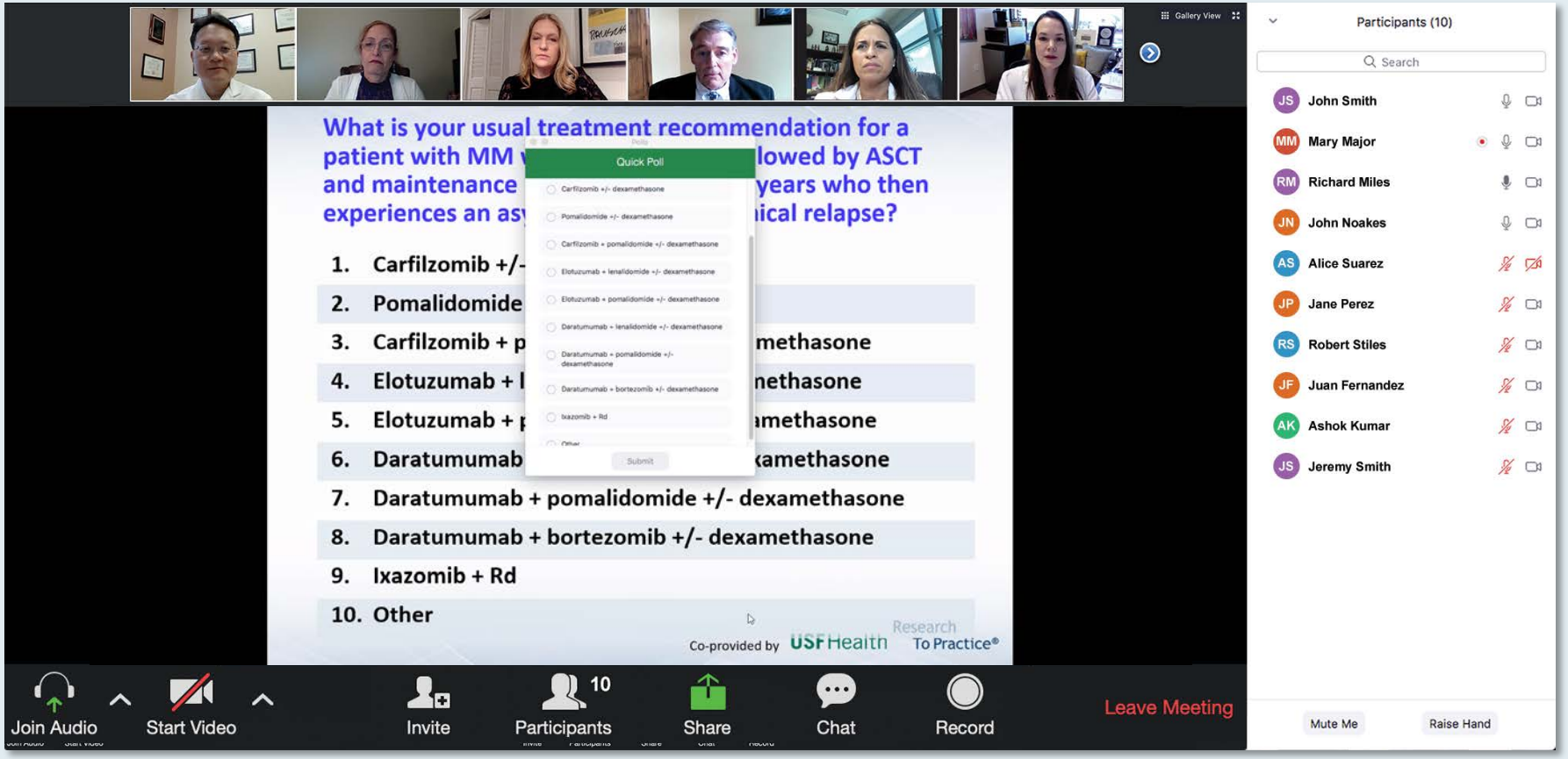

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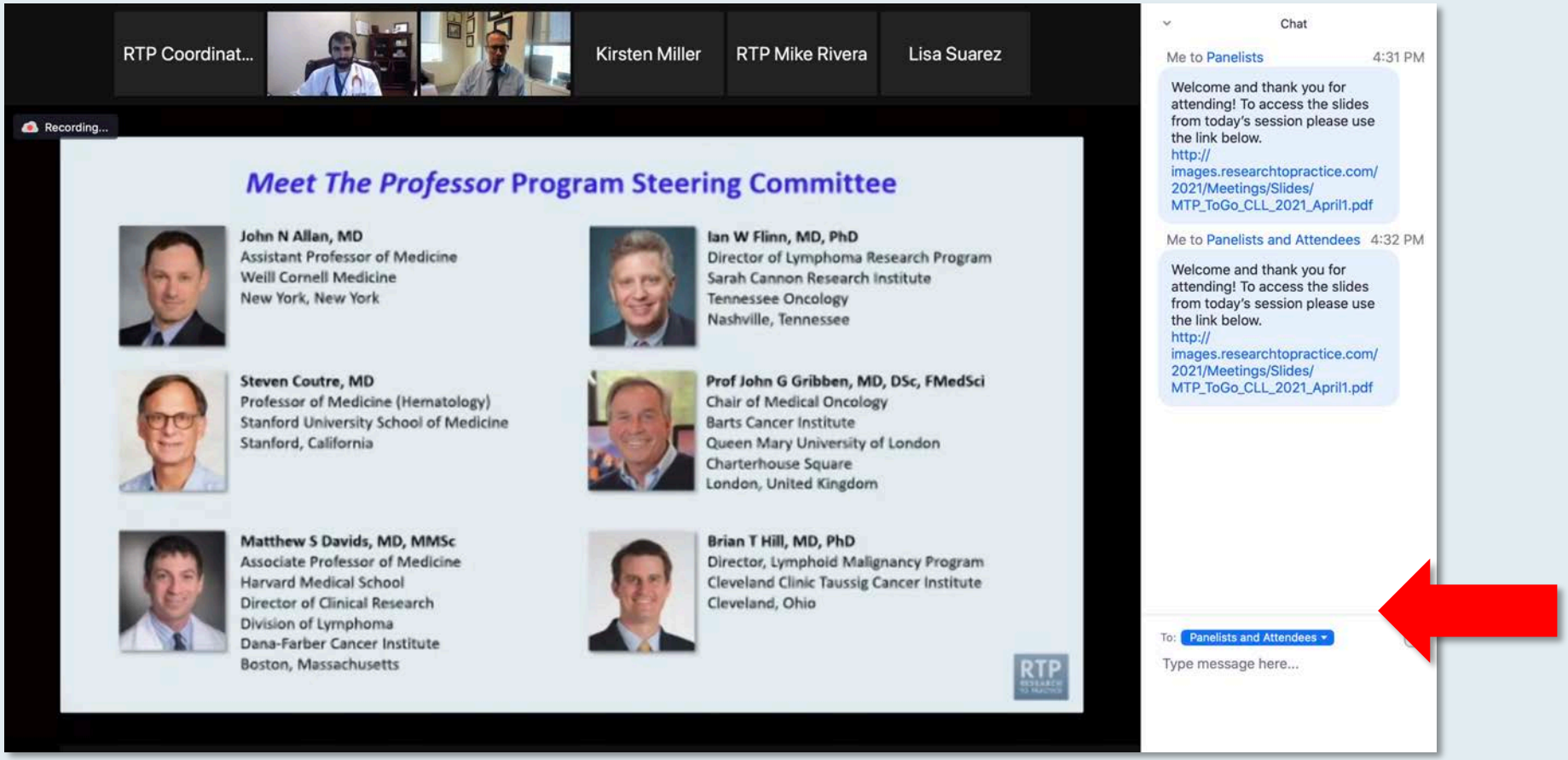

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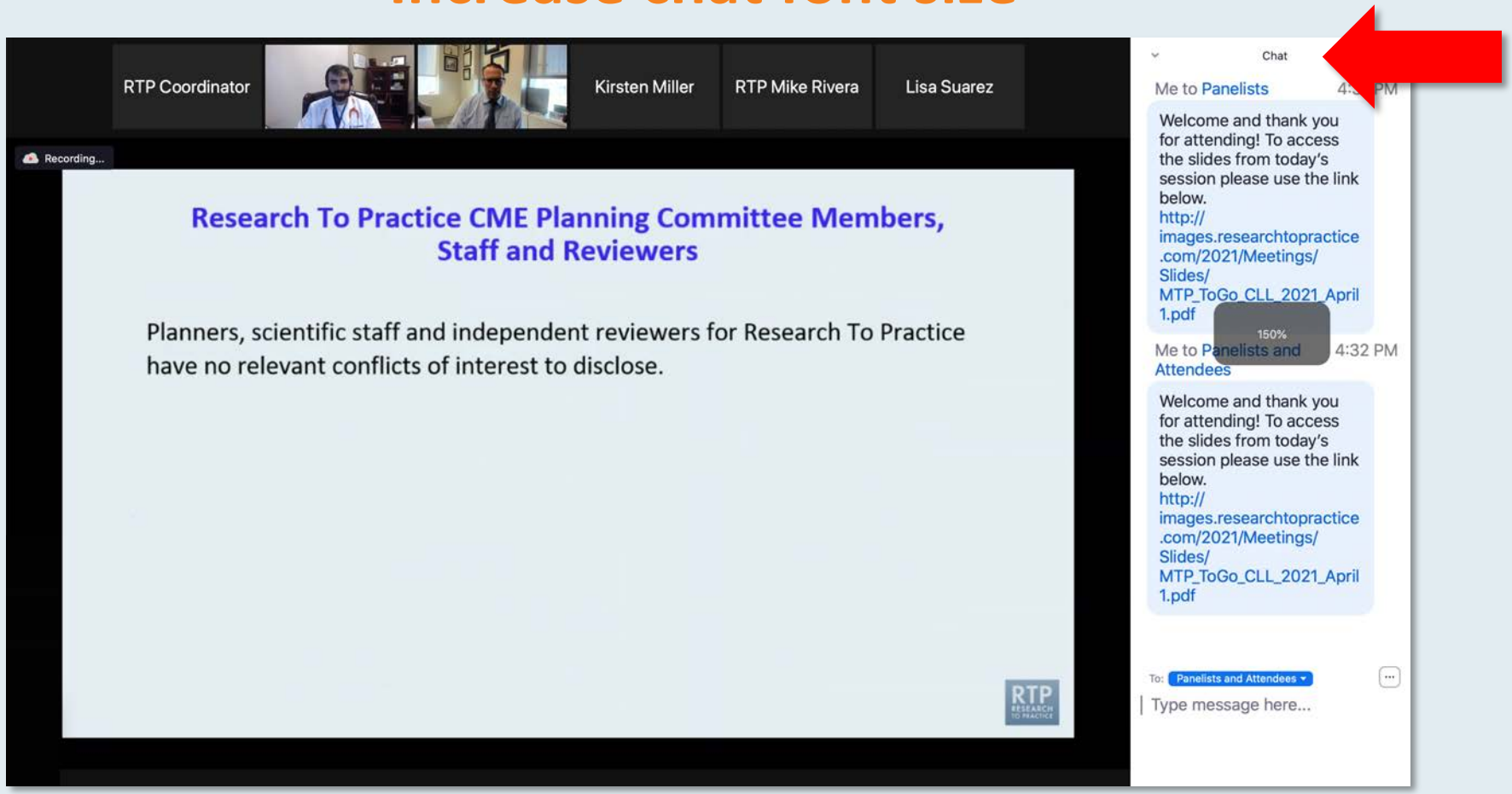

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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Key Presentations on Lung Cancer from the 2021 ASCO Annual Meeting

DR JOEL NEAL

STANFORD UNIVERSITY

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What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
11:00 AM – 12:30 PM ET

Faculty

Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD
Robert Svatek, MD

Moderator

Neil Love, MD

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Maha Hussain, MD, FACP, FASCO
A Oliver Sartor, MD
Neal D Shore, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Tuesday, September 14, 2021
5:00 PM – 6:00 PM ET

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Neeraj Agarwal, MD

Moderator

Neil Love, MD

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Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 16, 2021
5:00 PM – 6:00 PM ET

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Loretta J Nastoupil, MD

Moderator

Neil Love, MD

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Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Friday, September 17, 2021
12:00 PM – 1:00 PM ET

Faculty

Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Wednesday, September 22, 2021
5:00 PM – 6:00 PM ET

Faculty

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

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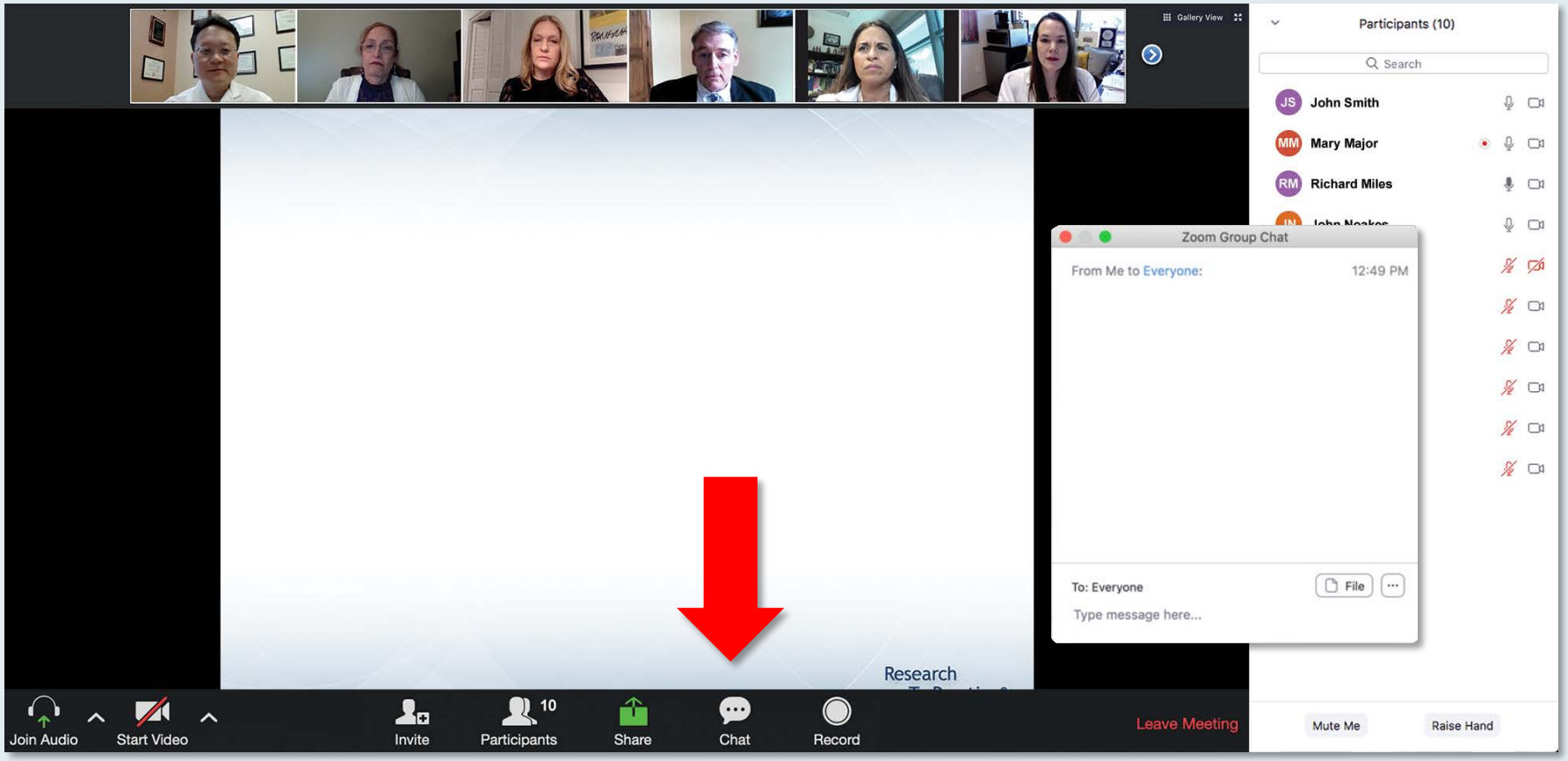

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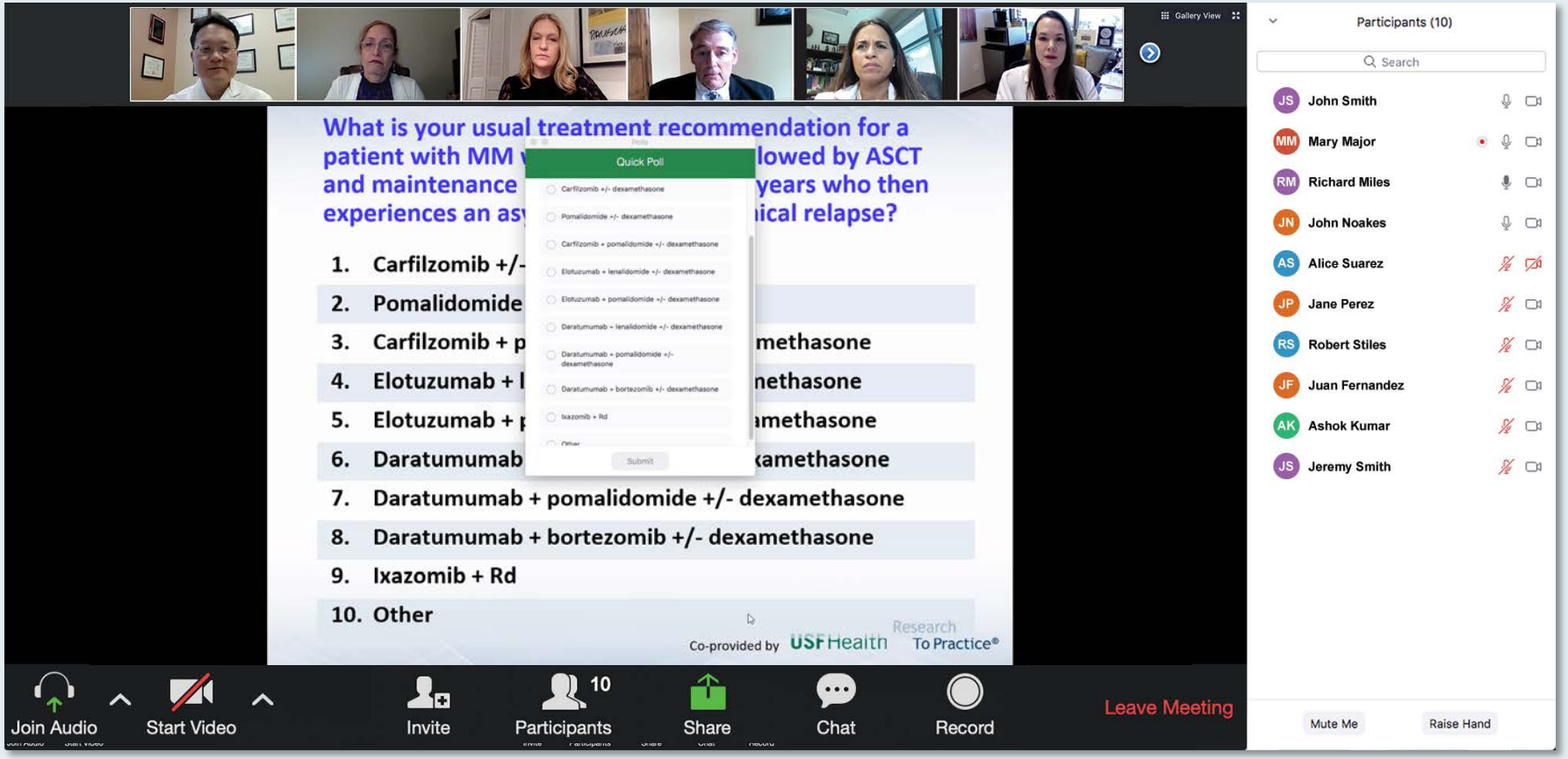

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Adjunct Assistant Professor of Oncology
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Agenda

Introduction: Tumor Board Discussions Since ASCO 2021?

Module 1: Immunotherapy in Surgically Resectable Non-Small Cell Lung Cancer

- Case: A 62-year-old woman with Stage IIA lung adenocarcinoma – PD-L1-negative, pan-wild type
- Case: A 56-year-old man with Stage IIA squamous NSCLC – PD-L1 15%
- Case: A 90-year-old man with Stage IB lung adenocarcinoma – PD-L1 10%
- Key relevant data sets

Module 2: Adjuvant Treatment of NSCLC with a Driver Mutation

- Case: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation
- Case: A 49-year-old woman with Stage IIIA lung adenocarcinoma – PD-L1 50%, ALK mutation
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May 2020

Adjuvant Chemotherapy

Jessica A. Hellyer, MD, Heather A. Wakelee, MD*

KEYWORDS

• Adjuvant • Chemotherapy • Targeted agents

KEY POINTS

- Standard of care for resectable, early-stage lung cancer is 4 cycles of adjuvant chemotherapy.
- Chemotherapy regimens have equitable efficacy, although in practice platinum plus pemetrexed is used most often for nonsquamous non–small cell lung cancer (NSCLC) due to favorable toxicity profile, with recent support for this approach from the JIPANG trial.
- Adjuvant immunotherapy is under investigation and discussed separately.
- Targeted therapies currently are not standard-of-care adjuvant treatment in driver mutation–positive early-stage NSCLC, but several trials are under way examining their use.

Thorac Surg Clin **2020;30(2):179-185.**

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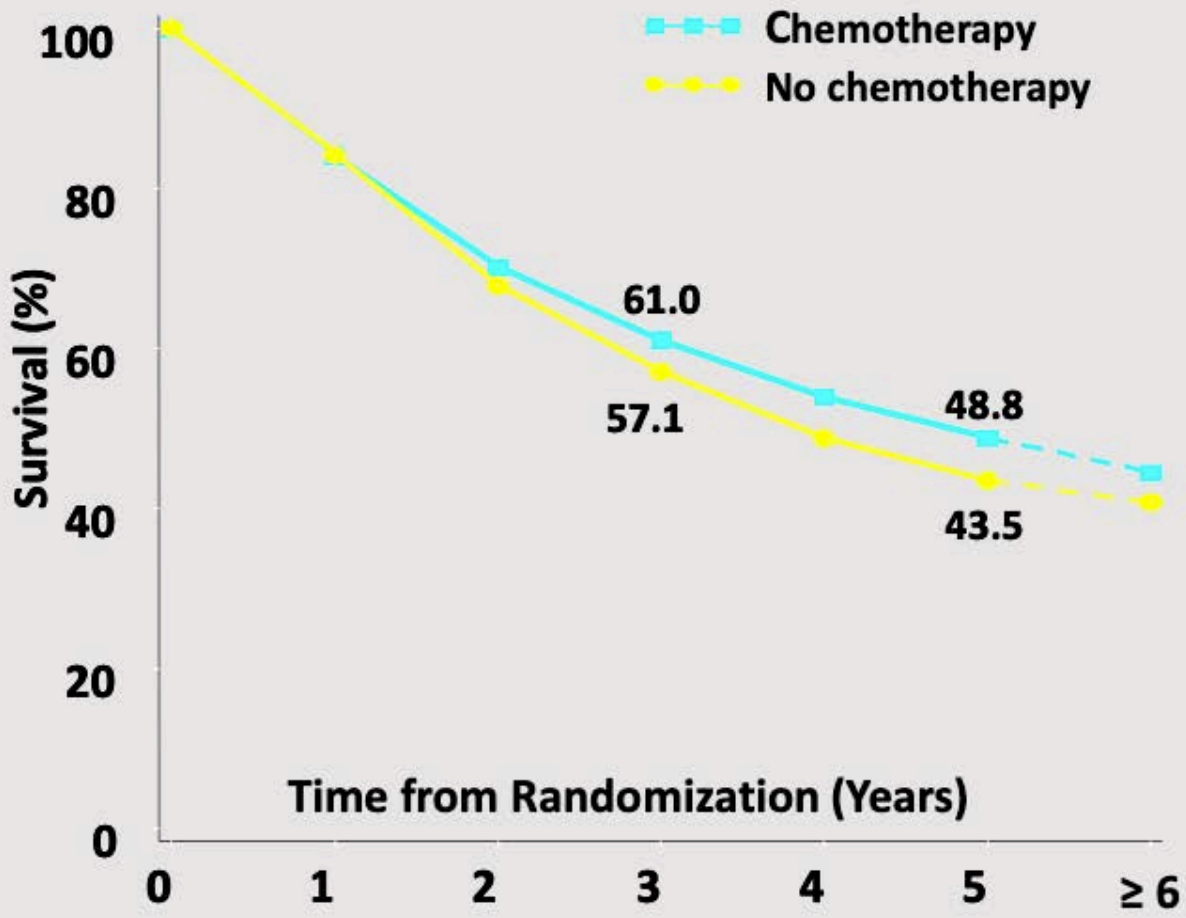
IO in the Surgically Resectable Patient

Jamie E. Chaft, MD
Memorial Sloan Kettering Cancer Center
USA

IASLC | 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Abstract PL05.04

We need to move beyond perioperative chemotherapy…



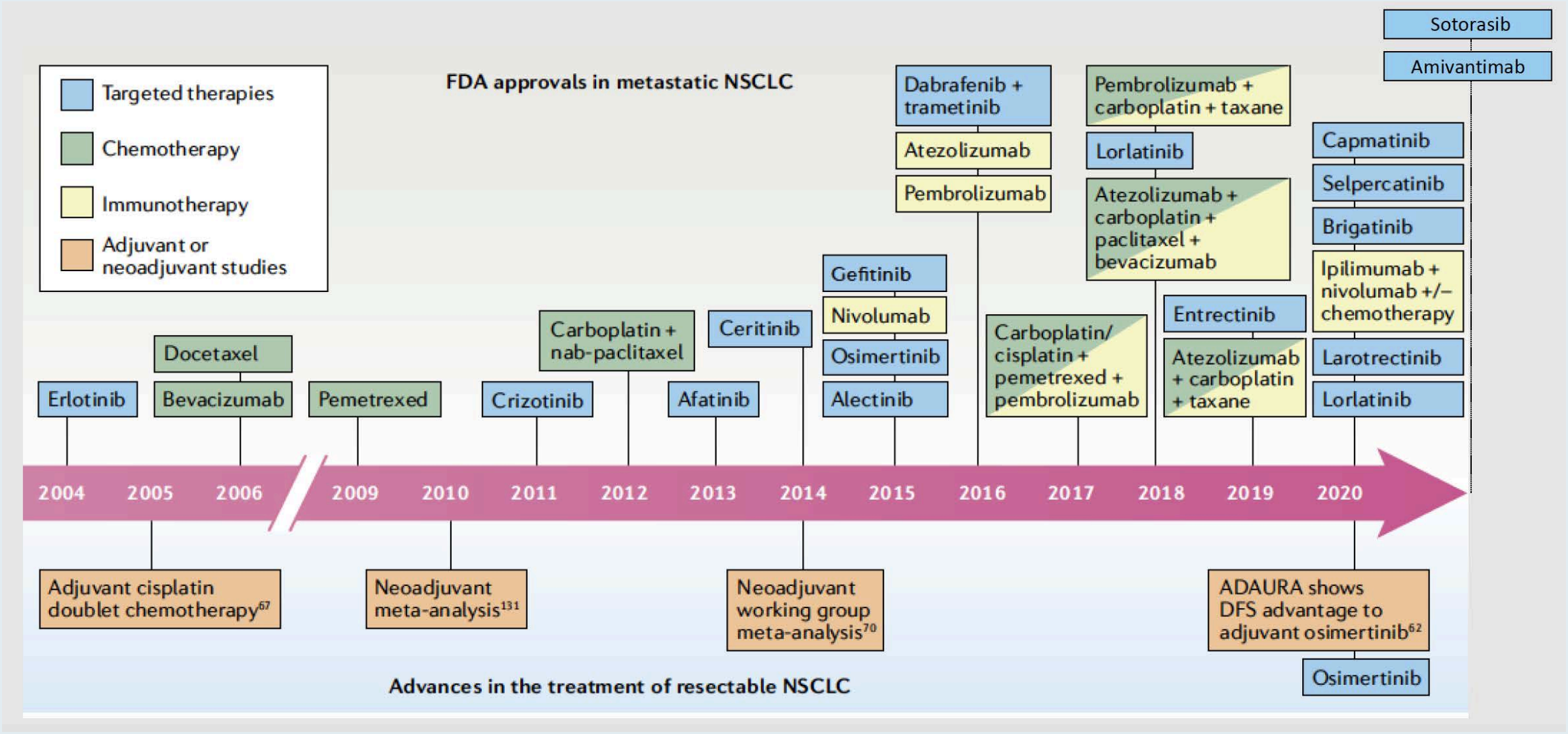
5.3% survival benefit at 5 years

HR = 0.89, $P < 0.005$

Pignon JP et al. J Clin Oncol 2008 Jul 20;26(21):3552-9

Chaft JE. IASLC 2021;Abstract PL05.04

Chasing Progress in Metastatic NSCLC



Chaft JE. IASLC 2021;Abstract PL05.04

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What about adjuvant IO?

- >4,650 patients enrolled
- All studies enrolled after SOC chemo
- All studies enrolled irrespective of PD-L1, however subsets planned
- Only 1 study powered for OS

Chaft JE. IASLC 2021;Abstract PL05.04

Ongoing Adjuvant PD-1/PD-L1 IO trials

Drug/Trial	Description	Stages entered	Description	Primary endpoint
Nivolumab	US, NCI (ECOG), Observational control	IB (4cm)-IIIA After Adj Chemo +/- radiation	Phase 3 Allows PD-L1 +/-	OS/DFS
Atezolizumab	Global, Placebo controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS
Durvalumab	Global, Placebo controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS
Pembrolizumab	ETOP/EORTC, Placebo Controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS

Courtesy of Heather Wakelee, MD

2021 ASCO ANNUAL MEETING

Abstract 8500

IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC)

Heather A. Wakelee,[1] Nasser Altorki,[2] Caicun Zhou,[3] Tibor Csőszi,[4] Ihor O. Vynnychenko,[5] Oleksandr Goloborodko,[6] Alexander Luft,[7] Andrey Akopov,[8] Alex Martinez-Marti,[9] Hirotsugu Kenmotsu,[10] Yuh-Min Chen,[11] Antonio Chella,[12] Shunichi Sugawara,[13] Fan Wu,[14] Jing Yi,[15] Yu Deng,[15] Mark McCleland,[15] Elizabeth Bennett,[15] Barbara J. Gitlitz,[15] Enriqueta Felip[16]

AACR American Association for Cancer Research

Abstract CT003

Nivolumab + platinum-doublet chemotherapy vs chemotherapy as neoadjuvant treatment for resectable (IB-IIIA) non-small cell lung cancer in the phase 3 CheckMate 816 trial

Patrick M. Forde,[1] Jonathan Spicer,[2] Shun Lu,[3] Mariano Provencio,[4] Tetsuya Mitsudomi,[5] Mark M. Awad,[6] Enriqueta Felip,[7] Stephen Broderick,[1] Julie Brahmer,[1] Scott J. Swanson,[6] Keith Kerr,[8] Changli Wang,[9] Gene B. Saylors,[10] Fumihiro Tanaka,[11] Hiroyuki Ito,[12] Ke-Neng Chen,[13] Cecile Dorange,[14] Junliang Cai,[14] Joseph Fiore,[14] Nicolas Girard[15]

Neoadjuvant/Adjuvant Immunotherapy for Curing Nondriver Genes

PD-(L)1 Checkpoint inhibitors:
Neoadjuvant: Improve surgical and pathologic outcomes
Adjuvant: Improve DFS in stage II-IIIA with PD-L1 expression

Becoming new Standard of Care for Early Stage NSCLC without a driver mutation

Likely will lead to improved cure rates

Wakelee HA. IASLC 2021;Abstract WS06.04

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Case Presentation: A 62-year-old woman with Stage IIA lung adenocarcinoma – PD-L1-negative, pan-wild type

Dr Jarushka Naidoo

- Incidental finding of a 7-cm right-sided lung mass with no other areas of metastatic disease after she presents to the ER after a motor vehicle accident
- NGS: No actionable mutations; PD-L1 assay: Negative
- Resection → Stage IIA, T3N02a

Questions

- When do you think mature data in terms of overall survival will be available for IMpower010?
- May we use the 22C3 assay for assessing PD-L1 status for patients where administration of atezolizumab is planned?
- Are there any data available on patients who have relapsed after atezolizumab, what are the patterns of relapse? Does administering immunotherapy early change the natural history of lung cancer in some way?

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ctDNA as a biomarker for treatment selection

Dr Jarushka Naidoo

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Case Presentation: A 56-year-old man with Stage IIA squamous NSCLC – PD-L1 15%

Dr Jarushka Naidoo

- Smoker who attends a lung cancer screening clinic is found to have a 4-cm right-sided lung mass on non-contrast CT
  - PET-CT identifies an FDG-avid right hilar lymph node, squamous NSCLC
  - Stage IIA, T2bN1
  - PD-L1: 15%

Questions

- Does PD-L1 score matter when deciding between a neoadjuvant and adjuvant approach for a patient? What are the cut-off values?
- What role does TMB play in your decision-making?

Role of surgery after neoadjuvant therapy

Dr Jarushka Naidoo

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Case Presentation: A 90-year-old man with Stage IB lung adenocarcinoma – PD-L1 10%

Dr Jarushka Naidoo

- Multiple medical comorbidities, ECOG PS 2
- He undergoes right upper lobe lobectomy for a Stage IB adenocarcinoma
- PD-L1 assay: 10%
- He has a slow postoperative recovery and returns for next appointment 10 weeks later

Questions

- What adjuvant treatment would you have recommended for this patient?
- From IMpower010, what do we know about the efficacy of atezolizumab in the Stage IB patient population?
- For this patient with multiple medical comorbidities in a poor performance status, should we think about adapting the algorithm and giving the patient atezolizumab alone and forgoing the chemotherapy?

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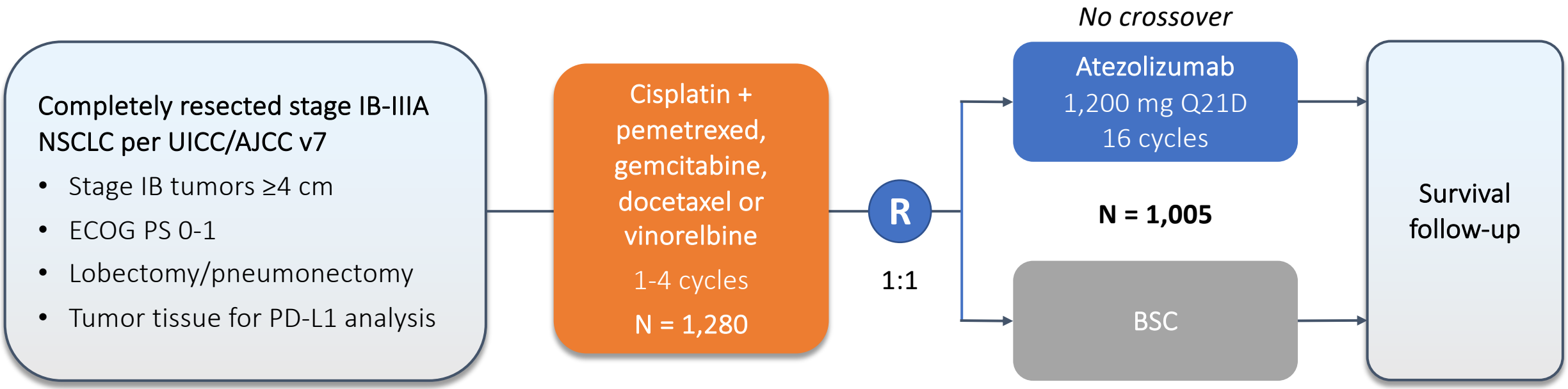
IO in the Surgically Resectable Patient

Considerations for Future Studies

- IO clearly has a role in early-stage lung cancer!
- Adenocarcinoma and Squamous cell carcinoma are different diseases and should be studied separately
- NGS is needed to understand impact of all drivers, not just *EGFR* and *ALK*, particularly in the adjuvant setting where time to test is ample
- We need to compare preop IO to postop IO, not default to give both as 4 randomized phase 3 studies are doing

Chaft JE. IASLC 2021;Abstract PL05.04

Phase 3 IMpower010 Study: Schema



Stratification factors

- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints

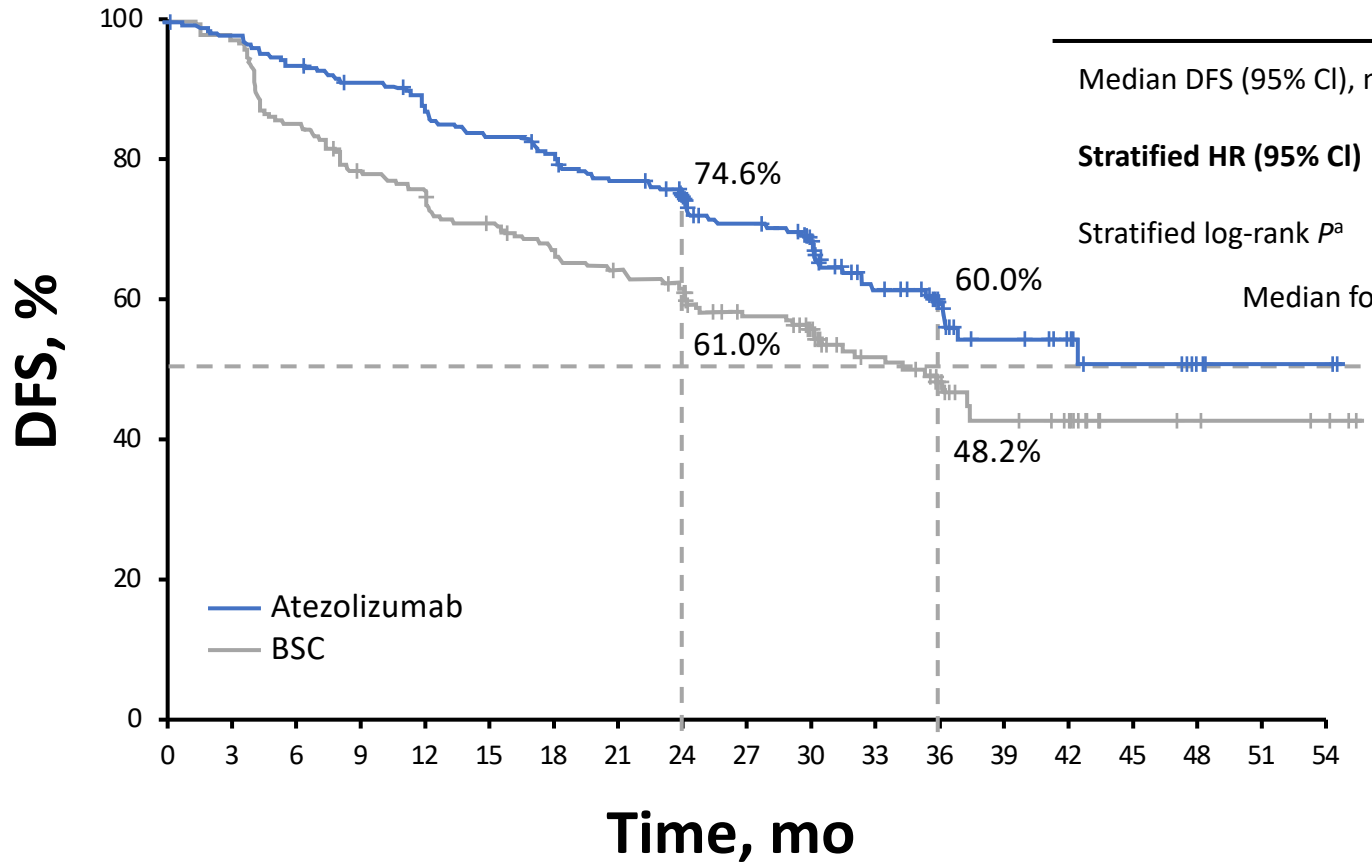
- Investigator-assessed DFS tested hierarchically:
  - PD-L1, TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Exploratory endpoints

- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-year and 5-year DFS in all 3 populations

Wakelee HA. ASCO 2021; Abstract 8500

IMpower010: DFS in the PD-L1 TC ≥1% Stage II-IIIA Population (Primary Endpoint)



	Atezolizumab n = 248	BSC n = 228
Median DFS (95% CI), mo	NE (36.1-NE)	35.3 (29.0-NE)
Stratified HR (95% CI)	**0.66 (0.50-0.88)**	
Stratified log-rank *P*[a]	.004[b]	

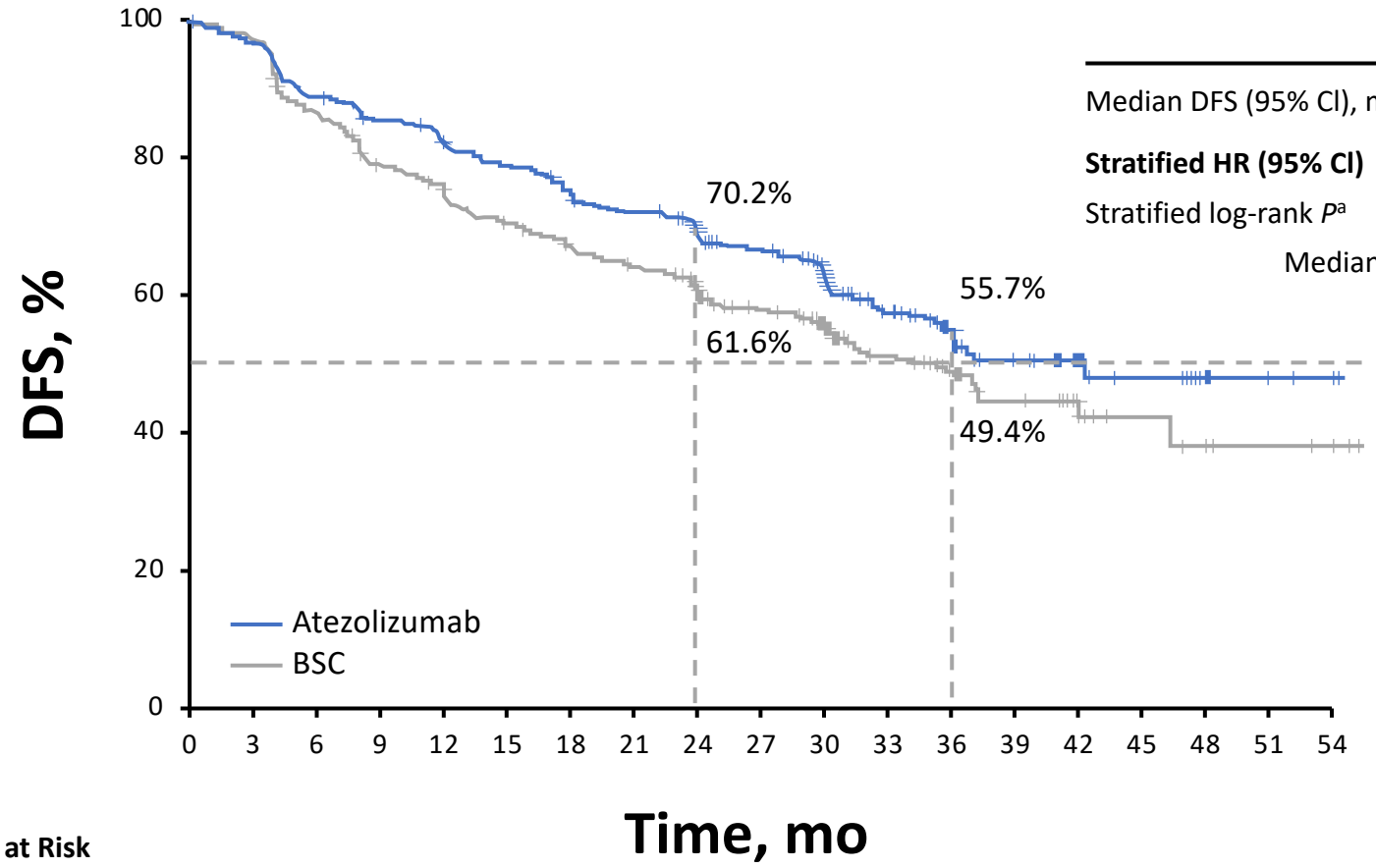
Median follow-up: 32.8 mo (range = 0.1-57.5)

No. at Risk

Atezolizumab	248	235	225	217	206	198	190	181	159	134	111	76	54	31	22	12	8	3	3
BSC	228	212	186	169	160	151	142	135	117	97	80	59	38	21	14	7	6	4	3

Wakelee HA. ASCO 2021; Abstract 8500

IMpower010: DFS in the All-Randomized Stage II-IIIA Population (Primary Endpoint)



	Atezolizumab N = 442	BSC N = 440
Median DFS (95% CI), mo	42.3 (36-NE)	35.3 (30.4-46.4)
Stratified HR (95% CI)	**0.79 (0.64-0.96)**	
Stratified log-rank *P*[a]	.02	

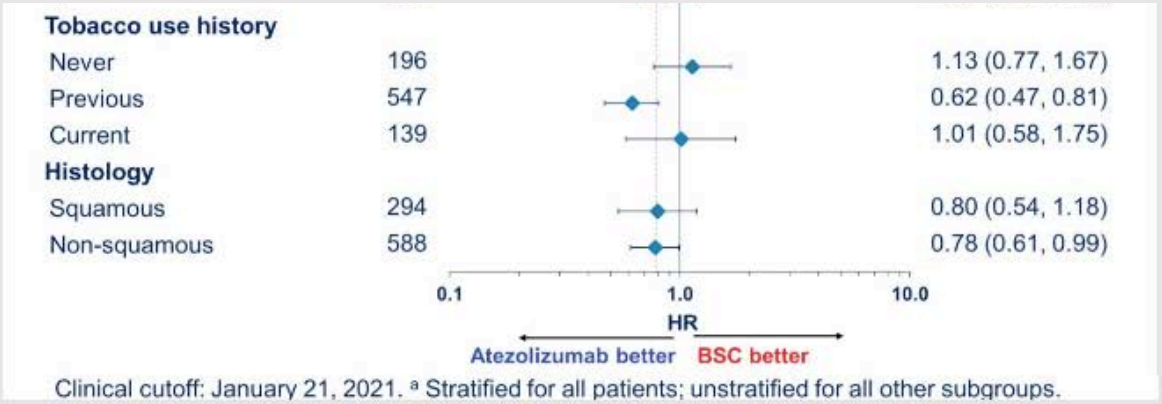
Median follow-up: 32.2 mo (range = 0-57.5)

No. at Risk

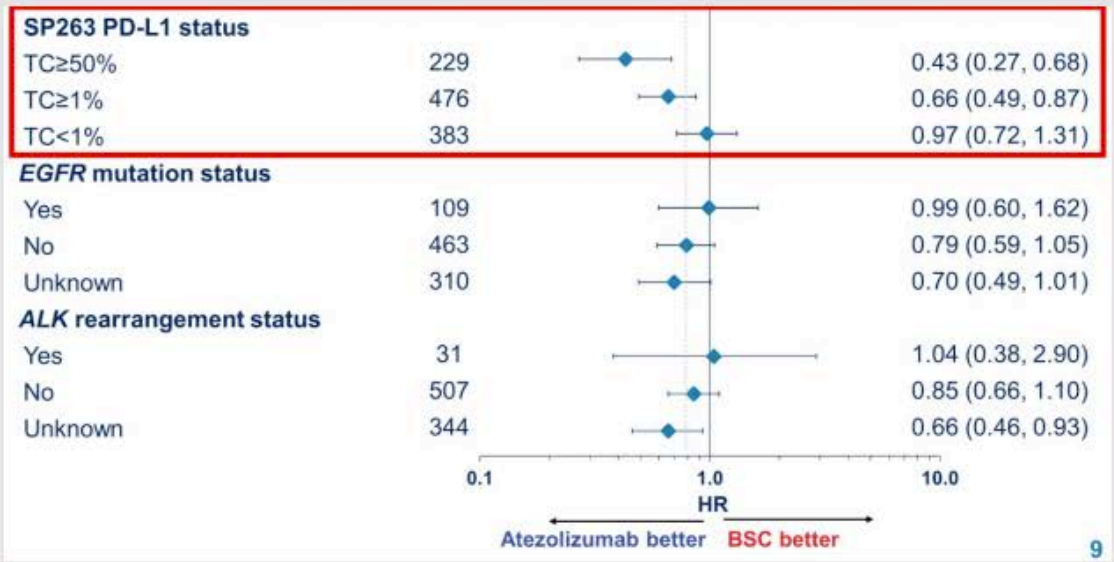
Atezolizumab	442	418	384	367	352	337	319	305	269	225	185	120	84	48	34	16	11	5	3
BSC	440	412	366	331	314	292	277	263	230	182	146	102	71	35	22	10	8	4	3

Wakelee HA. ASCO 2021; Abstract 8500

IMpower010: DFS in NSCLC ≥5cm (7th ed. St II-III) Key Subsets



Clinical cutoff: January 21, 2021. [a] Stratified for all patients; unstratified for all other subgroups.



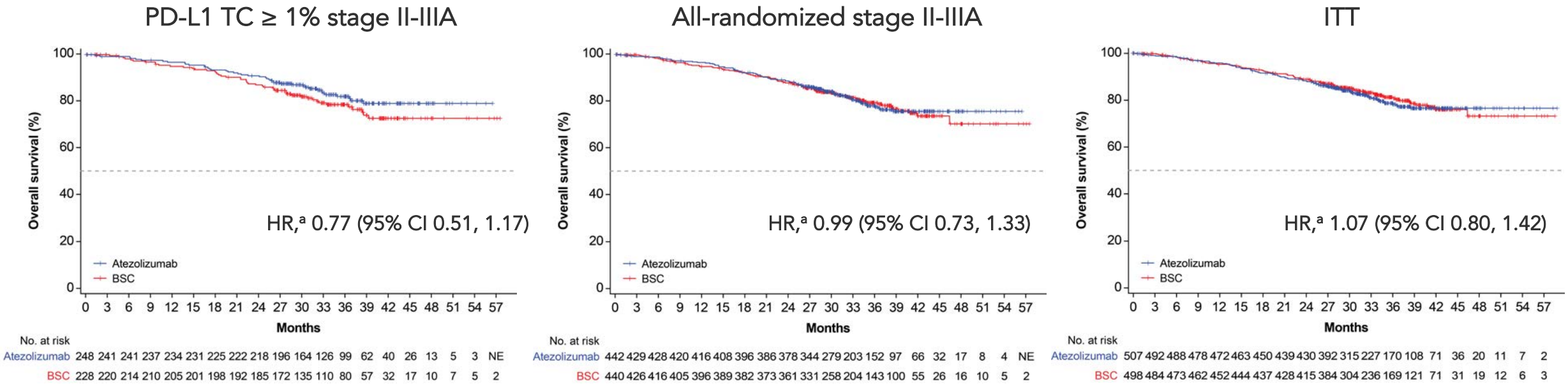
No obvious benefit in:

- Never smokers
- PD-L1 negative
- EGFR/ALK+

Adapted from Wakelee H et al. ASCO 2021;Abstract 8500

Chaft JE. IASLC 2021;Abstract PL05.04

IMpower010: early OS data at interim DFS analysis



OS data were immature at this pre-planned DFS interim analysis

OS in the ITT population was not formally tested

A trend toward OS improvement with atezolizumab was seen in the PD-L1 TC ≥1% stage II-IIIA population

Clinical cutoff: January 21, 2021. [a] Stratified.

Wakelee HA. ASCO 2021; Abstract 8500

Courtesy of Heather Wakelee, MD

IMpower010: Characterization of Stage IB-IIIA NSCLC Patients by Type and Extent of Therapy Prior to Adjuvant Atezolizumab

Nasser Altorki,[1] Enriqueta Felip,[2] Caicun Zhou,[3] Eric Vallieres,[4] Vladimir Moiseyenko,[5] Alexey Smolin,[6] Achim Rittmeyer,[7] Roman Vereshchako,[8] Maurice Perol,[9] Wolfgang Schutte,[10] Jian Fang,[11] Min Tao,[12] Encarnacao Teixeira,[13] Young-Chul Kim,[14] Virginia McNally,[15] Fan Wu,[16] Yu Deng,[17] Elizabeth Bennett,[17] Barbara Gitlitz,[17] Heather Wakelee[18]

[1] New York-Presbyterian Hospital, Weill Cornell Medicine, New York, NY; [2] Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [3] Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China; [4] Swedish Cancer Institute, Seattle, WA; [5] GBUZ Saint Petersburg Clinical Research Center of Specialized Types of Care (Oncology), Saint Petersburg, Russia; [6] Principal Military Clinical Hospital n.a. N.N. Burdenko, Moscow, Russia; [7] Lungenfachklinik Immenhausen, Immenhausen, Germany; [8] Kyiv Railway Clinical Hospital #3 of Branch Health Center of the PJSC Ukrainian Railway, Kyiv, Ukraine; [9] Centre Léon Bérard, Lyon, France; [10] Krankenhaus Martha-Maria; Halle-Dolau gGmbH, Halle, Germany; [11] Beijing Cancer Hospital, Beijing, China; [12] First Affiliated Hospital of Soochow University, Jiangsu, China; [13] Centro Hospitalar de Lisboa Norte E.P.E – Hospital Pulido Valente, Lisbon, Portugal; [14] Chonnam National University Medical School, and CNU Hwasun Hospital, Jeollanam-do, South Korea; [15] F. Hoffmann-La Roche Ltd., Basel, Switzerland; [16] Roche (China) Holding Ltd, Shanghai, China; [17] Genentech Inc, South San Francisco, CA; [18] Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA

IASLC 2021 World Conference on Lung Cancer
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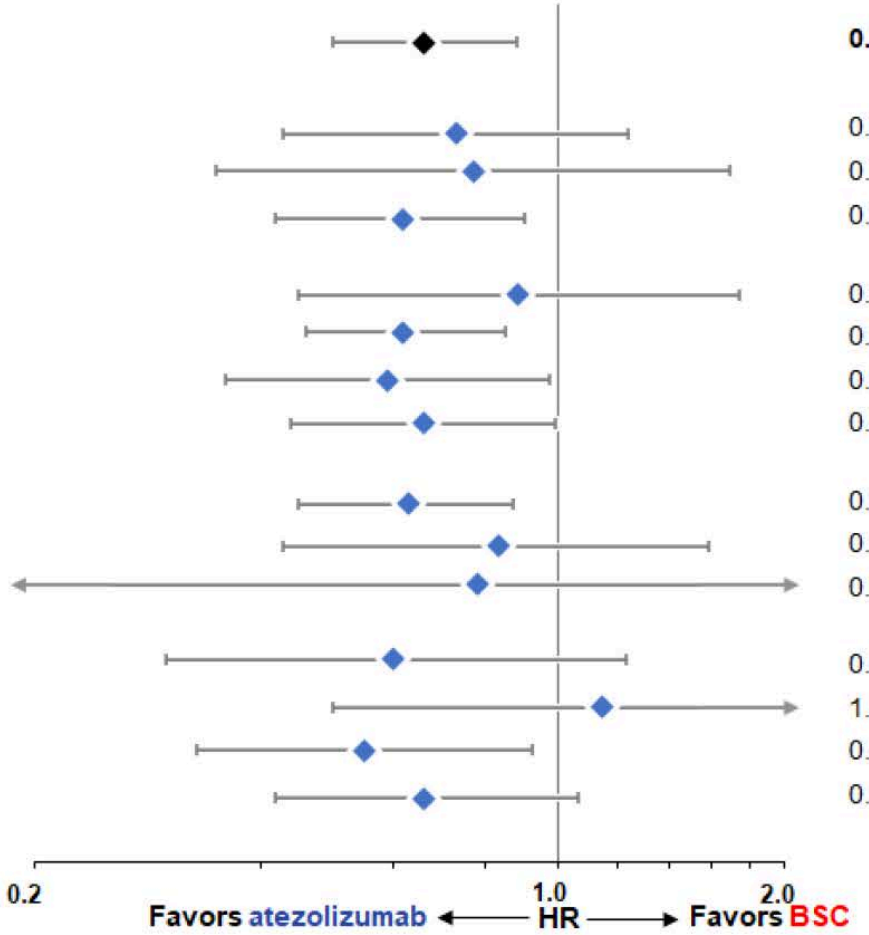
Abstract PL02.05

IMpower010: PD-L1 TC ≥1% Stage II-IIIA Population DFS by Disease and Treatment Characteristics

Subgroup	n	HR (95% CI)[b]	Median DFS, mo: Atezolizumab	Median DFS, mo: BSC
All patients	**476**	**0.66 (0.50, 0.88)**	**NE**	**35.3**
Disease stage				
Stage IIA	161	0.73 (0.43, 1.24)	NE	NE
Stage IIB	83	0.77 (0.35, 1.69)	NE	NE
Stage IIIA	232	0.62 (0.42, 0.90)	42.3	26.7
Regional lymph node status (pN)				
N0	106	0.88 (0.45, 1.74)	36.7	NE
N+	370	0.62 (0.46, 0.85)	NE	31.4
N1	194	0.59 (0.36, 0.97)	NE	NE
N2	176	0.66 (0.44, 0.99)	32.3	21.3
Type of surgery[c]				
Lobectomy	359	0.63 (0.45, 0.87)	NE	33.4
Pneumonectomy	85	0.83 (0.43, 1.58)	36.1	NE
Bilobectomy	24	0.78 (0.18, 3.33)	36.7	NE
Chemotherapy regimen				
Cisplatin-docetaxel	71	0.60 (0.30, 1.23)	36.1	18.0
Cisplatin-gemcitabine	75	1.14 (0.50, 2.61)	36.1	NE
Cisplatin-vinorelbine	161	0.55 (0.33, 0.92)	NE	34.2
Cisplatin-pemetrexed	169	0.66 (0.42, 1.06)	NE	31.4

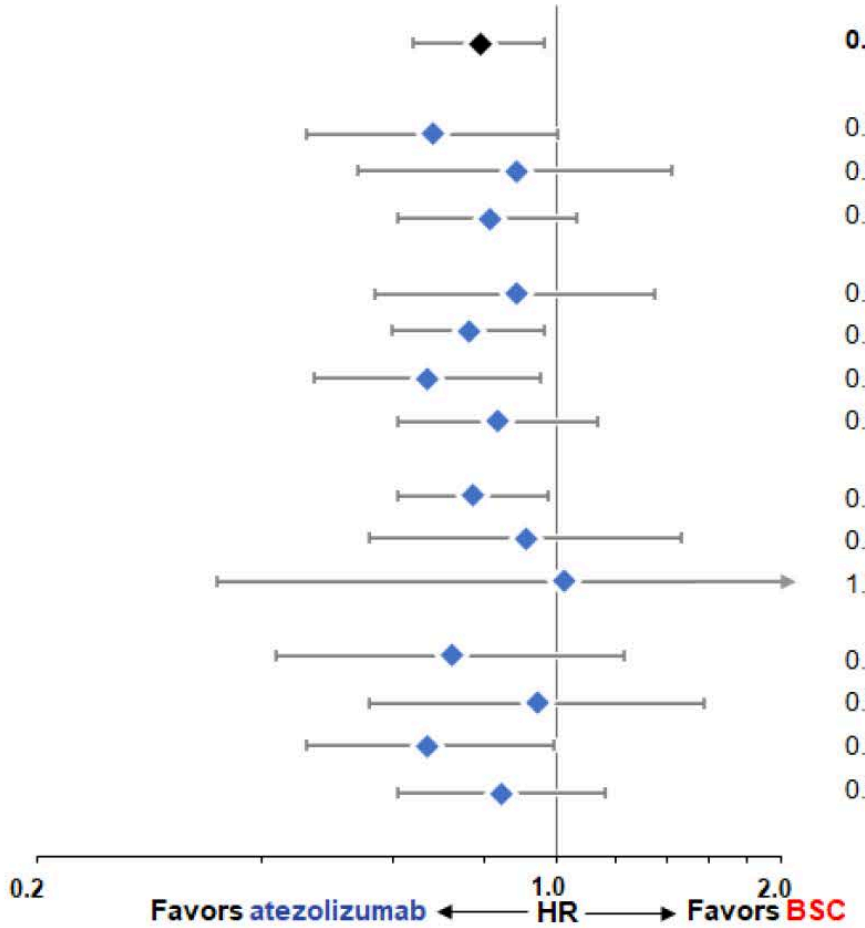


Clinical cutoff: January 21, 2021. [a] Per SP263 assay.
[b] Stratified for all patients; unstratified for all other subgroups.
[c] Subgroups with ≤10 patients are not shown.

Altorki N et al. IASLC 2021;Abstract PL02.05

IMpower010: All-Randomized Stage II-IIIA Population DFS by Disease and Treatment Characteristics

Subgroup	n	HR (95% CI)[a]	Median DFS, mo: Atezolizumab	Median DFS, mo: BSC
All patients	**882**	**0.79 (0.64, 0.96)**	**42.3**	**35.3**
Disease stage				
Stage IIA	295	0.68 (0.46, 1.00)	NE	NE
Stage IIB	174	0.88 (0.54, 1.42)	37.1	46.4
Stage IIIA	413	0.81 (0.61, 1.06)	32.3	29.7
Regional lymph node status (pN)				
N0	229	0.88 (0.57, 1.35)	NE	46.4
N+	653	0.76 (0.60, 0.96)	42.3	31.4
N1	348	0.67 (0.47, 0.95)	NE	36.0
N2	305	0.83 (0.61, 1.13)	30.2	24.1
Type of surgery[b]				
Lobectomy	675	0.77 (0.61, 0.97)	42.3	32.0
Pneumonectomy	150	0.91 (0.56, 1.47)	36.1	42.1
Bilobectomy	47	1.02 (0.35, 2.98)	36.7	NE
Chemotherapy regimen				
Cisplatin-docetaxel	124	0.72 (0.42, 1.23)	36.1	37.3
Cisplatin-gemcitabine	138	0.94 (0.56, 1.57)	36.1	46.4
Cisplatin-vinorelbine	271	0.67 (0.46, 0.99)	NE	37.0
Cisplatin-pemetrexed	349	0.84 (0.61, 1.16)	42.3	31.4

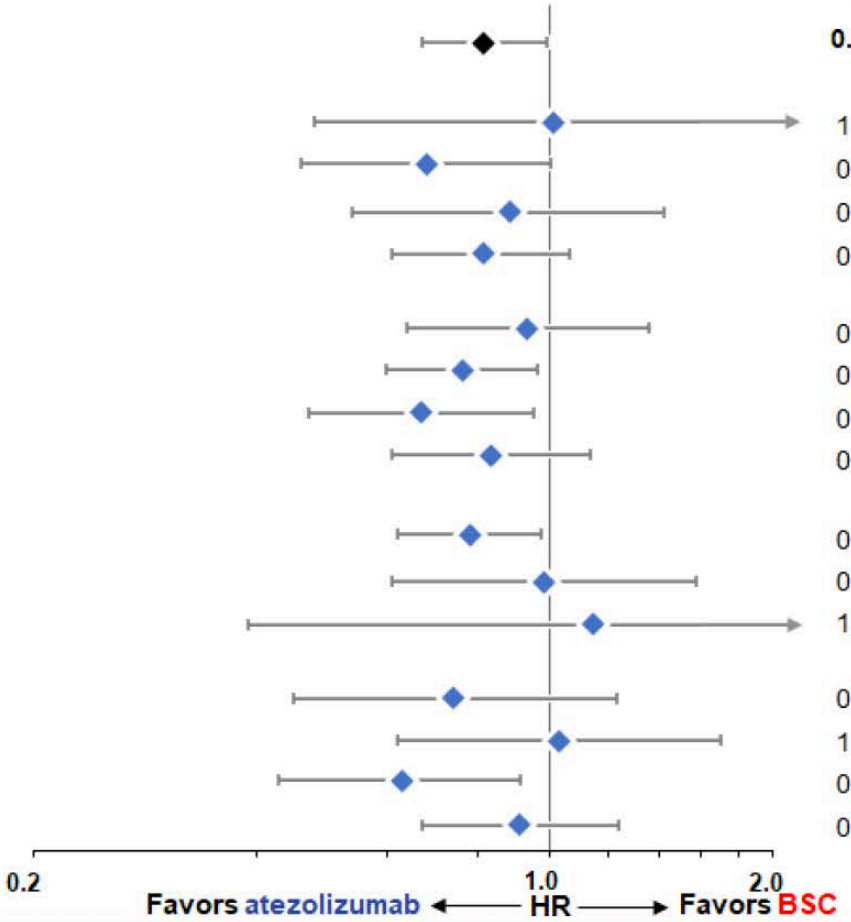


Clinical cutoff: January 21, 2021.
[a] Stratified for all patients; unstratified for all other subgroups.
[b] Subgroups with ≤10 patients are not shown.

Altorki N et al. IASLC 2021;Abstract PL02.05

IMpower010: ITT (All-Randomized Stage IB-IIIA) Population DFS by Disease and Treatment Characteristics

Subgroup	n	HR (95% CI)[a]	Median DFS, mo: Atezolizumab	Median DFS, mo: BSC
All patients	**1005**	**0.81 (0.67, 0.99)[b]**	**NE**	**37.2**
Disease stage				
Stage IB	123	1.01 (0.48, 2.13)	NE	NE
Stage IIA	295	0.68 (0.46, 1.00)	NE	NE
Stage IIB	174	0.88 (0.54, 1.42)	37.1	46.4
Stage IIIA	413	0.81 (0.61, 1.06)	32.3	29.7
Regional lymph node status (pN)				
N0	352	0.93 (0.64, 1.36)	NE	NE
N+	653	0.76 (0.60, 0.96)	42.3	31.4
N1	348	0.67 (0.47, 0.95)	NE	36.0
N2	305	0.83 (0.61, 1.13)	30.2	24.1
Type of surgery[c]				
Lobectomy	785	0.78 (0.62, 0.97)	NE	36.0
Pneumonectomy	160	0.98 (0.61, 1.57)	36.1	42.1
Bilobectomy	50	1.14 (0.39, 3.34)	36.7	NE
Chemotherapy regimen				
Cisplatin-docetaxel	152	0.74 (0.45, 1.23)	36.1	42.1
Cisplatin-gemcitabine	165	1.03 (0.62, 1.70)	36.7	46.4
Cisplatin-vinorelbine	303	0.63 (0.43, 0.91)	NE	37.0
Cisplatin-pemetrexed	385	0.91 (0.67, 1.24)	42.3	36.0



Clinical cutoff: January 21, 2021. [a] Stratified for all patients; unstratified for all other subgroups. [b] DFS did not cross the significance boundary in the ITT population. [c] Subgroups with ≤10 patients are not shown.

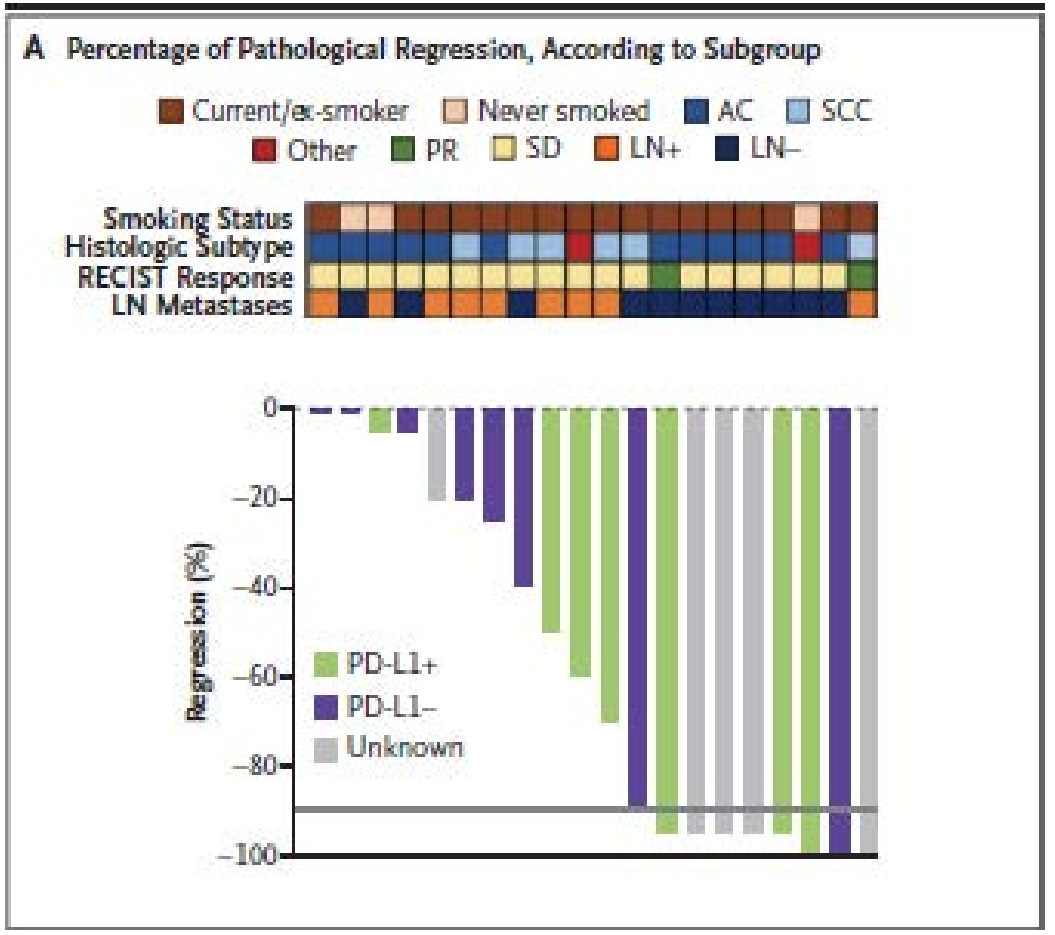
Altorki N et al. IASLC 2021;Abstract PL02.05

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

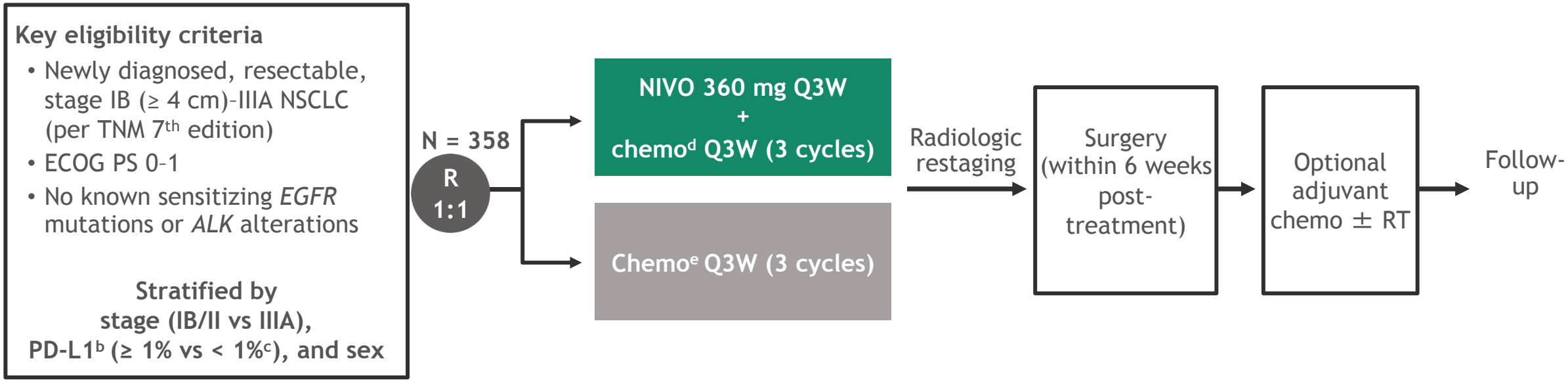
Neoadjuvant PD-1 Blockade in Resectable Lung Cancer

P.M. Forde, J.E. Chaft, K.N. Smith, V. Anagnostou, T.R. Cottrell, M.D. Hellmann, M. Zahurak, S.C. Yang, D.R. Jones, S. Broderick, R.J. Battafarano, M.J. Velez, N. Rekhtman, Z. Olah, J. Naidoo, K.A. Marrone, F. Verde, H. Guo, J. Zhang, J.X. Caushi, H.Y. Chan, J.-W. Sidhom, R.B. Scharpf, J. White, E. Gabrielson, H. Wang, G.L. Rosner, V. Rusch, J.D. Wolchok, T. Merghoub, J.M. Taube, V.E. Velculescu, S.L. Topalian, J.R. Brahmer, and D.M. Pardoll



Courtesy of Eric Vallieres, MD

CheckMate 816 Phase III study design



Primary endpoints
- pCR by BIPR
- EFS by BICR

Key secondary endpoints
- MPR by BIPR
- OS
- Time to death or distant metastases

Key exploratory endpoints included
- ORR by BICR
- **Feasibility of surgery; peri- and post-operative surgery-related AEs**

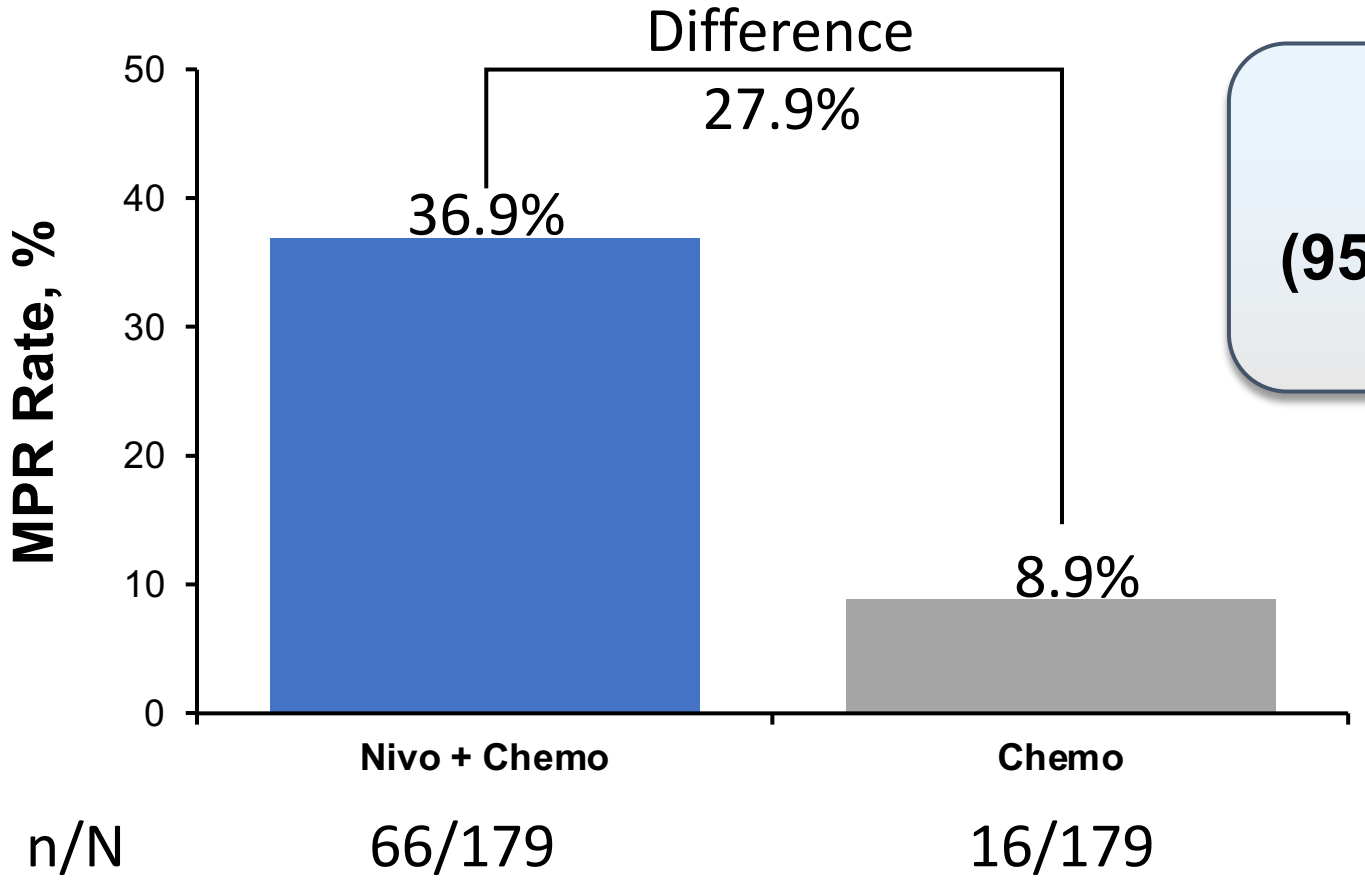
Database lock: September 16, 2020; minimum follow-up: 7.6 months for NIVO + chemo and chemo arms.

[a]NCT02998528; this study included an exploratory arm: NIVO 3 mg/kg Q2W (3 cycles) + ipilimumab 1 mg/kg (cycle 1 only). Data from this arm are not included in this presentation; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Included patients with PD-L1 expression status not evaluable and indeterminate; [d]NSQ: pemetrexed + cisplatin or paclitaxel + carboplatin; SQ: gemcitabine + cisplatin or paclitaxel + carboplatin; [e]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (SQ only), pemetrexed + cisplatin (NSQ only), or paclitaxel + carboplatin.

1. Forde PM, et al. Oral presentation at the AACR Annual Meeting; April 8–10, 2021; virtual. Abstract 5218.

Spicer J. ASCO 2021;Abstract 8503

CheckMate 816: MPR Rate in the ITT Population

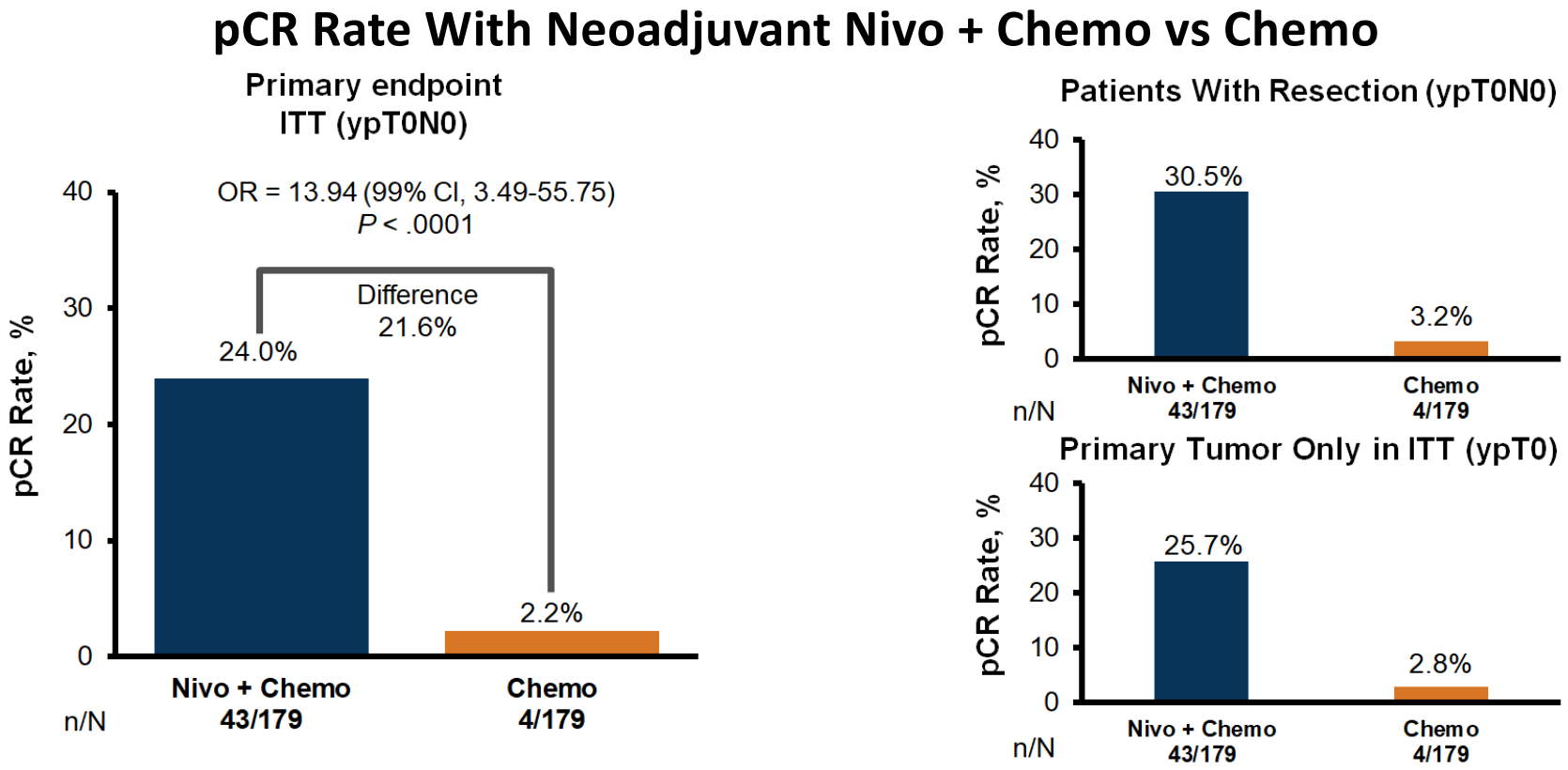


OR = 5.70
(95% CI, 3.16-10.26)

Spicer J. ASCO 2021;Abstract 8503

CheckMate 816: pCR Rate (Primary Endpoint)

- The addition of nivo to chemo increased pCR from 2.2% with chemo alone to 24% with chemo + nivo (*P* < .0001)
- pCR was assessed by central pathologists who were blinded to trial arms



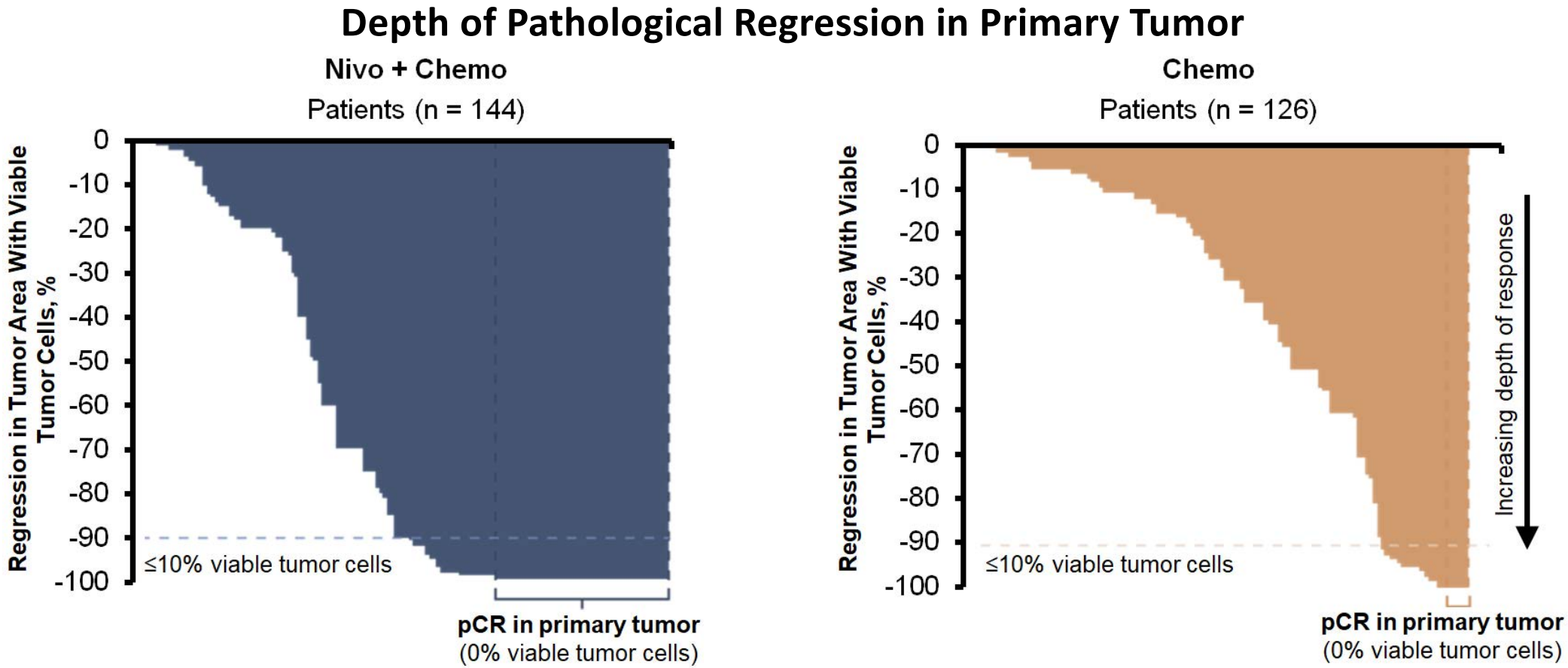
- **pCR rate in the exploratory nivo + ipi arm (ITT) was 20.4% (95% CI, 13.4-29.0)**

Forde PM et al. AACR 2021. Abstract CT003.

Courtesy of Brendan M Stiles, MD

CheckMate 816: Pathological Regression

- Surgical specimens had a median of 10% residual tumor cells after chemo + nivo vs 74% after chemo alone

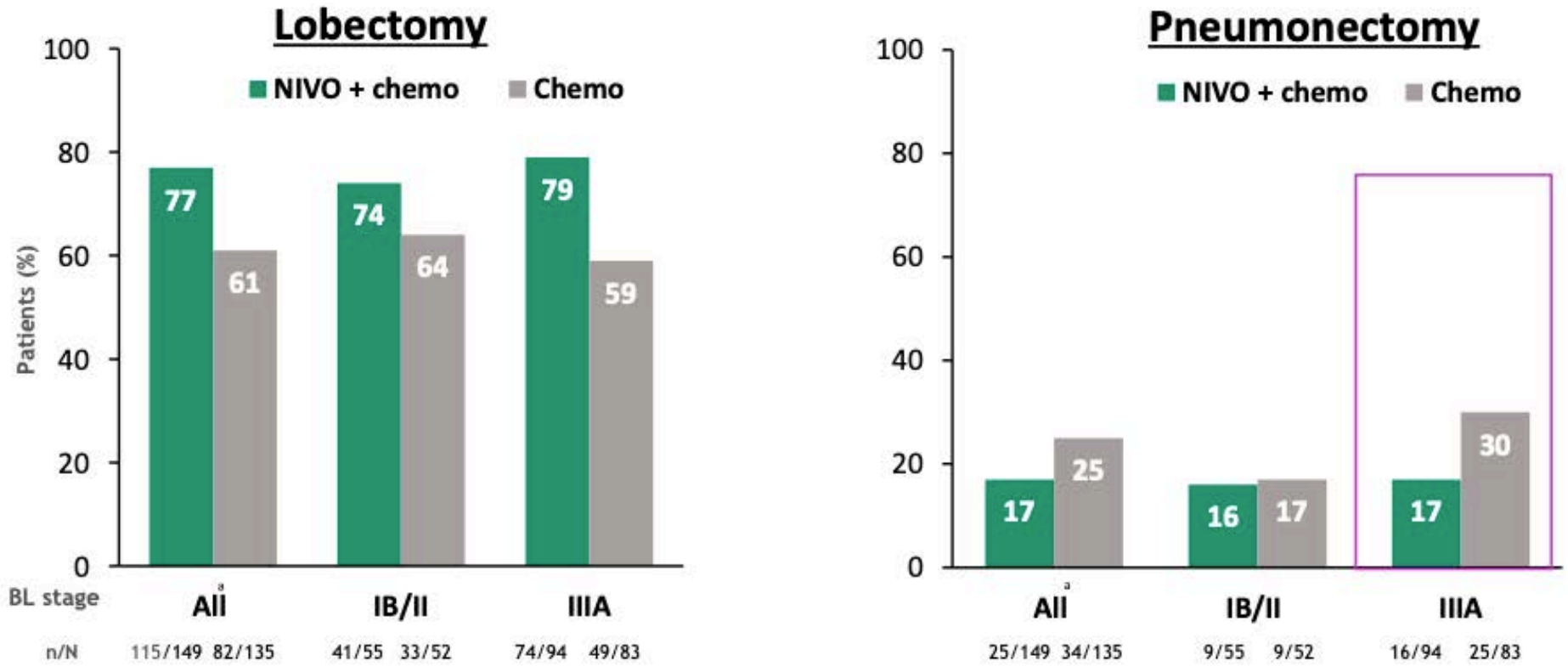


- **Median viable tumor cells were 10% in the nivo + chemo arm and 74% in the chemo arm**

Forde PM et al. AACR 2021. Abstract CT003.

Courtesy of Brendan M Stiles, MD

CheckMate 816: Type Of Surgery by Baseline Stage of Disease



Spicer J. ASCO 2021; Abstract 8503

Neoadjuvant pembrolizumab for early stage non-small cell lung cancer

Jair Bar[1], Damien Urban[1], Ilanit Redinsky[1], Aliza Ackerstein[1], Sameh Daher[1], Iris Kamer[1], Amir Onn[2], Tiberiu Shulimzon[2], Michael Peled[2], Nona Zeitlin[3], Ran Kremer[3], Stephen Raskin[4], Alon Ben-Nun[3], Marina Perelman[5], Efrat Ofek[5]

[1]Institute of Oncology, Sheba Medical Center, Tel HaShomer, Ramat Gan, Israel, [2]Institute of Pulmonology, Sheba Medical Center, Ramat Gan, Israel, [3]Thoracic Surgery, Sheba Medical Center, Ramat Gan, Israel, [4]Radiology Department, Sheba Medical Center, Ramat Gan, Israel, [5]Pathology Department, Sheba Medical Center, Ramat Gan, Israel

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Abstract OA11.01

Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer

TRAE grade ≥ 3

Pt. #19

72 yo male, past-light smoker. PMHx: CAF

Myositis grade 3 (day 9)
Myocarditis grade 3 (day 22)

Pt. #29

62 yo female, heavy smoker

Encephalitis grade 3 (day 124)
Hepatitis grade 3 (day 171)

All in the expansion cohort

AE leading to surgery deferral

Pt. #19

72 yo male, past-light smoker. PMHx: CAF

Myositis grade 3 (day 9)
Myocarditis grade 3 (day 22)

Pt. #18

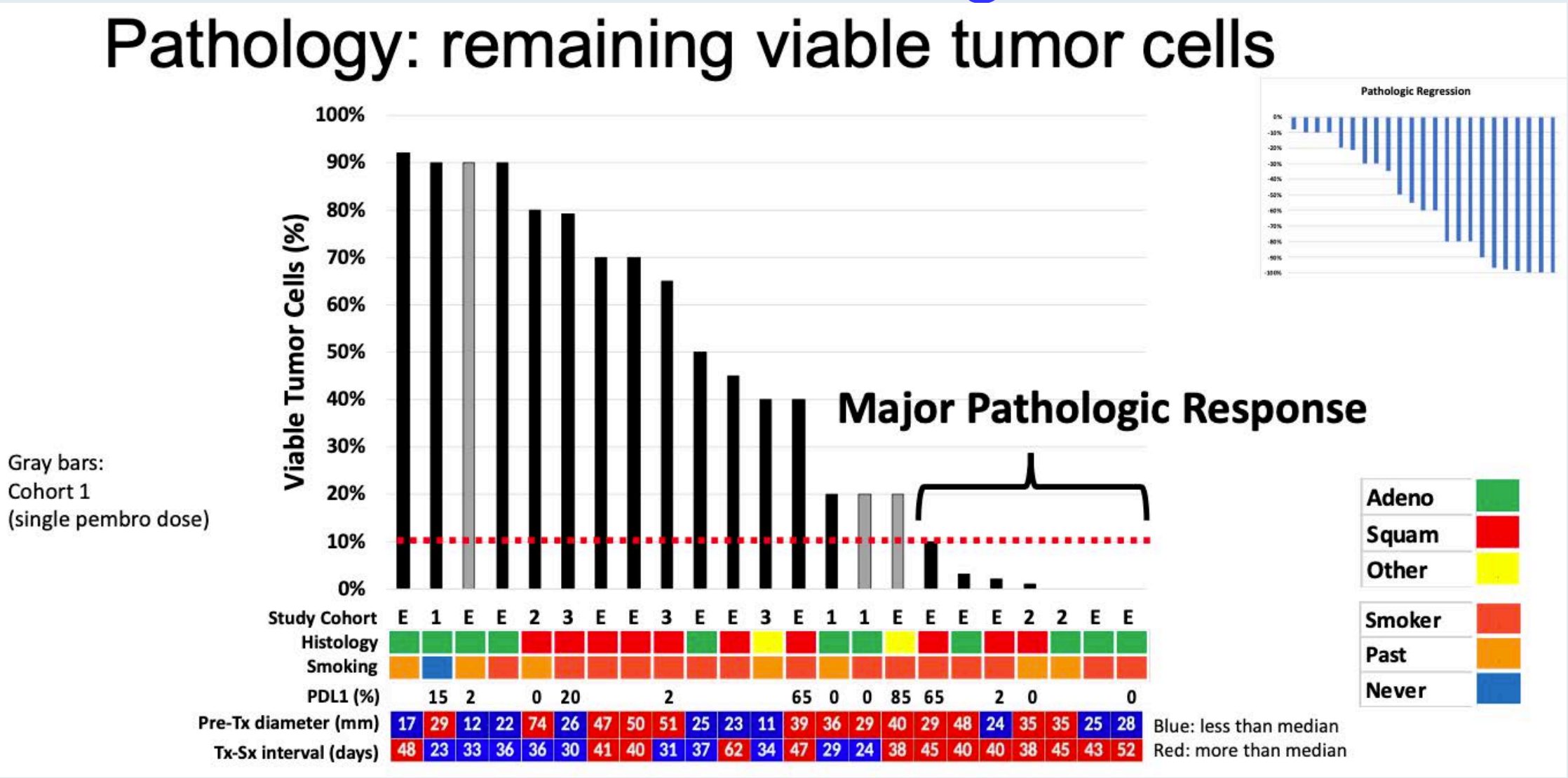
71 yo male, past heavy smoker. PMHx: DM2, HTN, diverticulosis

Myocardial infarct (day 21)

TRAE: treatment-related adverse events. Pt: patient. PMHx: past medical history. CAF: Chronic atrial fibrilation. DM: diabetes melitus type 2. HTN: hypertension.

Bar J et al. IASLC 2021;Abstract OA11.01

Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer



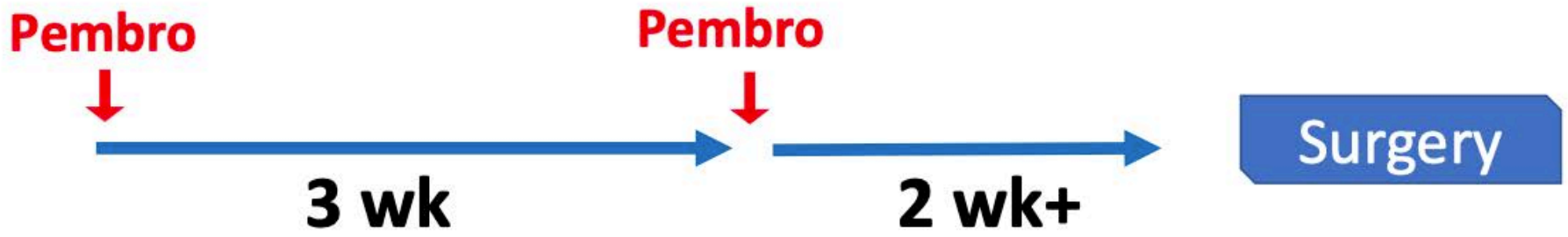
Bar J et al. IASLC 2021;Abstract OA11.01

RTP RESEARCH TO PRACTICE

Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer

Recommended Phase 2 Dose/Schedule

- No DLT in the escalation cohorts
- MPR was observed only in patients with a time interval from treatment initiation to surgery ≥ 5 weeks
- Recommended dose/schedule:



- Exploratory: among the patients treated by this dose/schedule (n=16)
  - MPR 44% (7 of 16)
  - pCR 19% (3 of 16)

Bar J et al. IASLC 2021;Abstract OA11.01

Neoadjuvant Pembrolizumab for Early Stage Non-Small Cell Lung Cancer

TAKE HOME MESSAGES

- Neoadjuvant Pembrolizumab was safe, with an 8% rate of grade 3-4 TRAE, with no apparent relation to treatment-surgery interval
- Outcome in the entire study cohort:
  - 27% rate of MPR (7 of 26)
  - 12% rate of pCR (3 of 26)
- Longer interval from treatment to surgery was associated with higher rate of MPR
- Two doses of neoadjuvant pembrolizumab at a three-week interval, followed by surgery at two weeks or later, is the RP2D/S
- Exploratory look at the patients treated by the RP2D/S reveals:
  - MPR 44% (7 of 16)
  - pCR 19% (3 of 16)

Bar J et al. IASLC 2021;Abstract OA11.01

Ongoing Phase 3 NEO-Adj PD-(L)1 NSCLC IO

Drug	N	Stages	Description	Primary Endpoint
Nivo + platinum Chemo (ipi/nivo closed) CheckMate 816	350	Stage IB–IIIA, resectable NSCLC	Neo-adjuvant, no adjuvant	MPR / RFS
Atezo + platinum Chemo IMpower030	374	Stage II–IIIB (T3N2), resectable NSCLC	Neo-adjuvant chemo-ICI, then adjuvant IO	MPR / RFS
Pembro + platinum-doublet Chemo KEYNOTE-671	786	Stage IIB–IIIA, resectable NSCLC	Neo-adjuvant chemo-ICI then adjuvant IO	RFS / OS
Durva + platinum-doublet Chemo	300	Stage II–IIIA, resectable NSCLC	Neo-adjuvant chemo-ICI then adjuvant IO	MPR

Courtesy of Heather Wakelee, MD

Agenda

Introduction: Tumor Board Discussions Since ASCO 2021?

Module 1: Immunotherapy in Surgically Resectable Non-Small Cell Lung Cancer

- Case: A 62-year-old woman with Stage IIA lung adenocarcinoma – PD-L1-negative, pan-wild type
- Case: A 56-year-old man with Stage IIA squamous NSCLC – PD-L1 15%
- Case: A 90-year-old man with Stage IB lung adenocarcinoma – PD-L1 10%
- Key relevant data sets

Module 2: Adjuvant Treatment of NSCLC with a Driver Mutation

- Case: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation
- Case: A 49-year-old woman with Stage IIIA lung adenocarcinoma – PD-L1 50%, ALK mutation
- Key relevant data sets

RTP RESEARCH TO PRACTICE

Case Presentation: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation

Dr Jarushka Naidoo

- S/p resection of a right hilar lesion and mediastinal lymph node dissection, which revealed a 5-cm lung adenocarcinoma with involvement of station 4R lymph nodes
- Stage III, pT2aN2
- PD-L1 assay: < 1%
- NGS: EGFR L858R mutation

Question

- What treatment approach would you recommended for this patient?

Case Presentation: A 68-year-old man with Stage III lung adenocarcinoma – PD-L1 <1%, EGFR L858R mutation (continued)

Dr Jarushka Naidoo

- S/p resection of a right hilar lesion and mediastinal lymph node dissection, which revealed a 5-cm lung adenocarcinoma with involvement of station 4R lymph nodes
- Stage III, pT2aN2
- PD-L1 assay: < 1%
- NGS: EGFR L858R mutation

Questions

- What treatment approach would you recommended for this patient?
- ***Would postoperative radiotherapy have been appropriate for this patient***?

RTP RESEARCH TO PRACTICE

Case Presentation: A 49-year-old woman with Stage IIIA lung adenocarcinoma – PD-L1 50%, ALK mutation

Dr Jarushka Naidoo

- Never smoker who presents to PCP with sudden onset dyspnea and is diagnosed with Stage IIIA, T2bN2 NSCLC
- NGS: ALK rearrangement
- PD-L1 assay: 50%
- Tumor is deemed resectable by the thoracic surgeon

Question

- What treatment option would you recommend for this patient?
- How do you interpret the PD-L1 score in a patient who is also positive for an ALK rearrangement?
- In light of the PACIFIC trial, what is your perspective on whether or not Stage III disease should undergo resection?

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

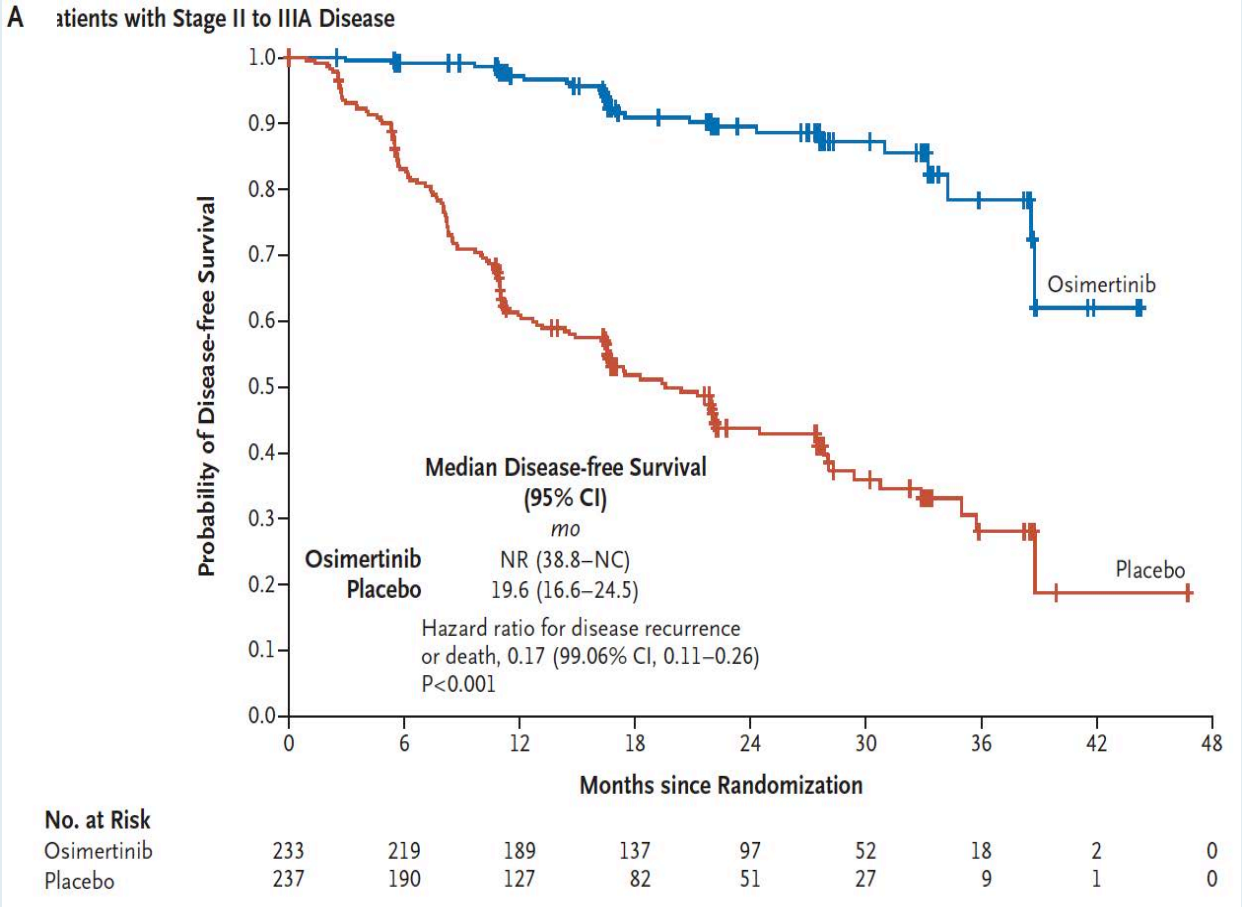
ORIGINAL ARTICLE

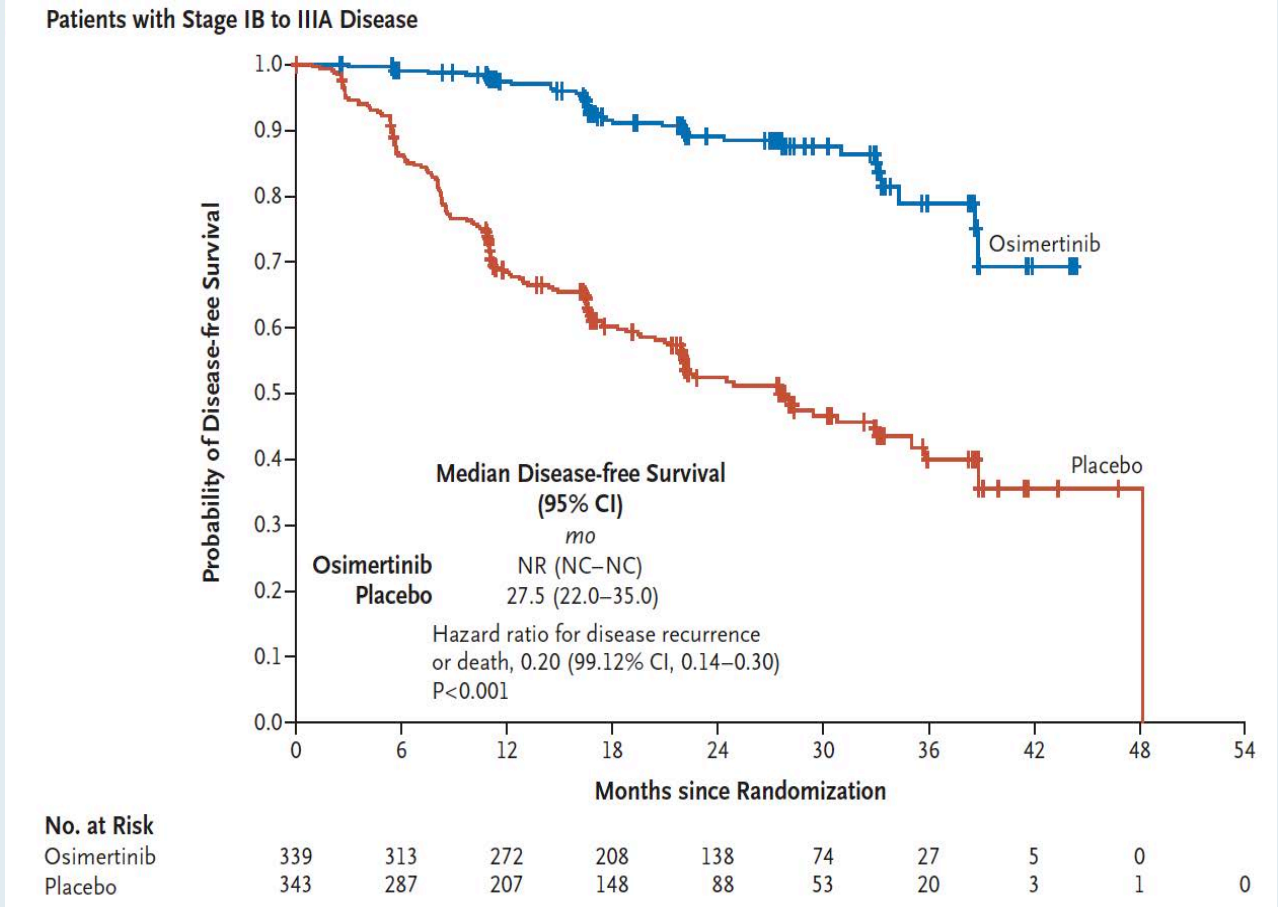
Osimertinib in Resected *EGFR*-Mutated Non–Small-Cell Lung Cancer

Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodge, M.Sc., Ajlan Atasoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D.,

N Engl J Med 2020;383(18):1711-23.

ADAURA: Disease-Free Survival by Stage





Wu YL et al. *N Engl J Med* 2020;383(18):1711-23.

RTP RESEARCH TO PRACTICE

ADAURA: Adjuvant Osimertinib in Resected Stage IB-IIIA EGFR+ NSCLC

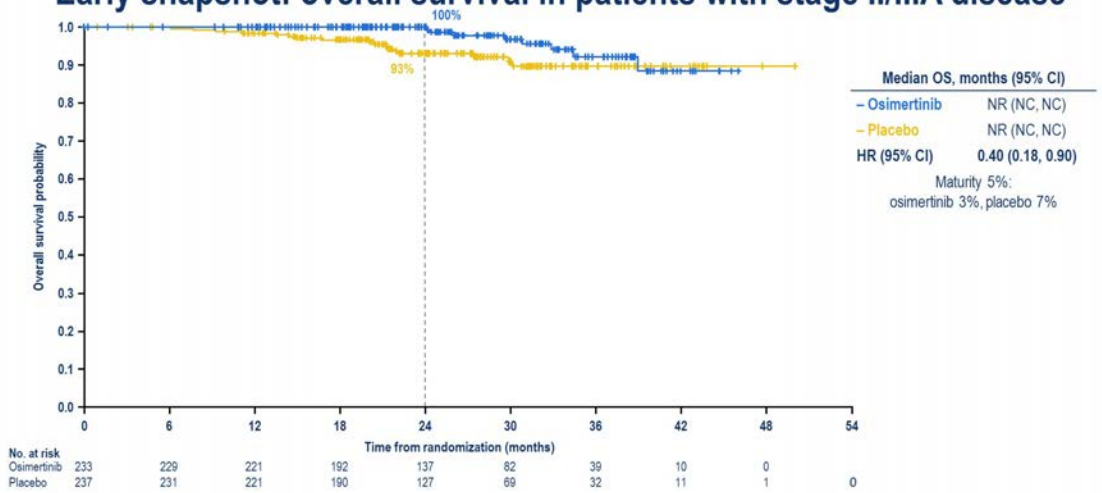
DFS by stage

	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	**0.50 (0.25, 0.96)**	**0.17 (0.08, 0.31)**	**0.12 (0.07, 0.20)**

- In the osimertinib arm, 2 year DFS rates were consistent across stages IB, II, and IIIA disease
- Maturity (overall population: stage IB / II / IIIA) 29%: osimertinib events 12%, placebo events 46%

DFS benefit increases consistently with stage

Early snapshot: overall survival in patients with stage II/IIIA disease



***OS remains very immature (5% maturity)**

Courtesy of Zofia Piotrowska, MD, MHS

Herbst R et al. ASCO 2020; Wu TL et al. NEJM 2020

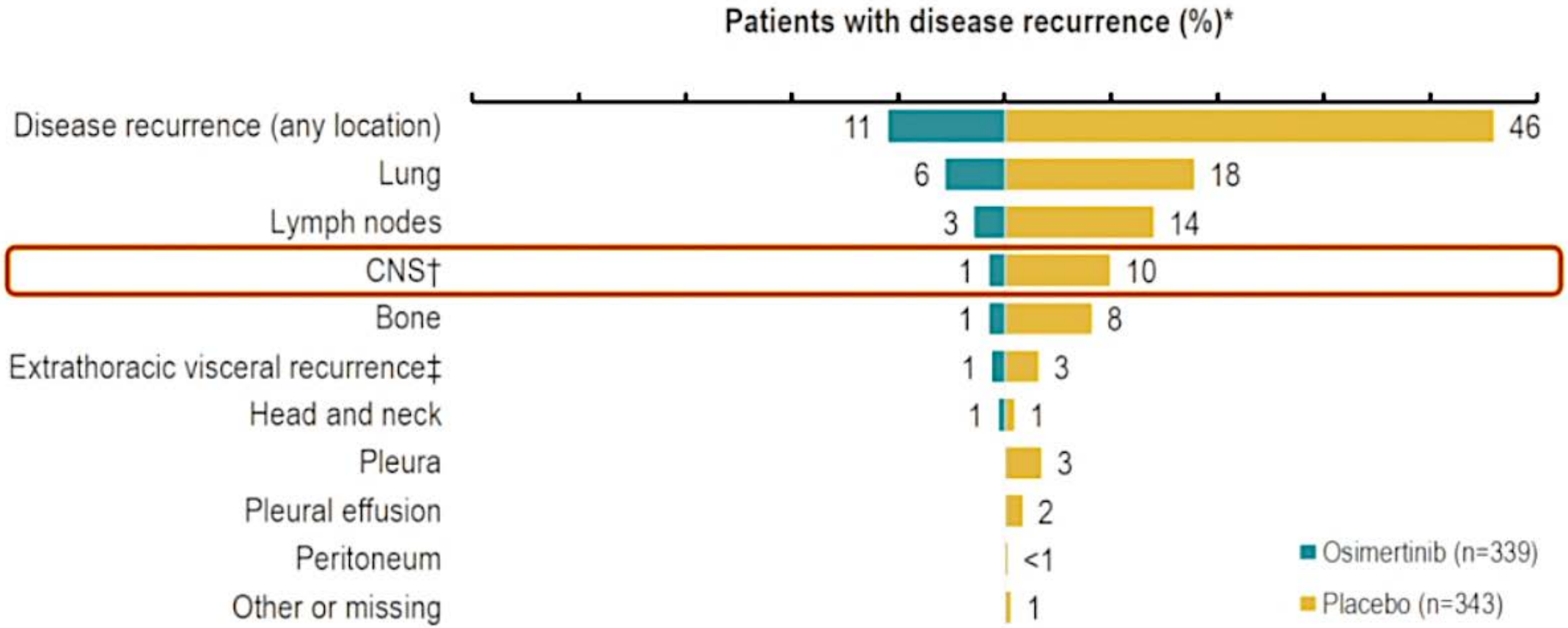
MASSACHUSETTS GENERAL HOSPITAL CANCER CENTER

Osimertinib Adjuvant Therapy in Patients (pts) with Resected EGFR Mutated (EGFRm) NSCLC (ADAURA): Central Nervous System (CNS) Disease Recurrence

Tsuboi M et al.

ESMO 2020;Abstract LBA1.

ADAURA: Sites of Disease Recurrence



Tsuboi M et al. ESMO 2020;Abstract LBA1.

RTP RESEARCH TO PRACTICE

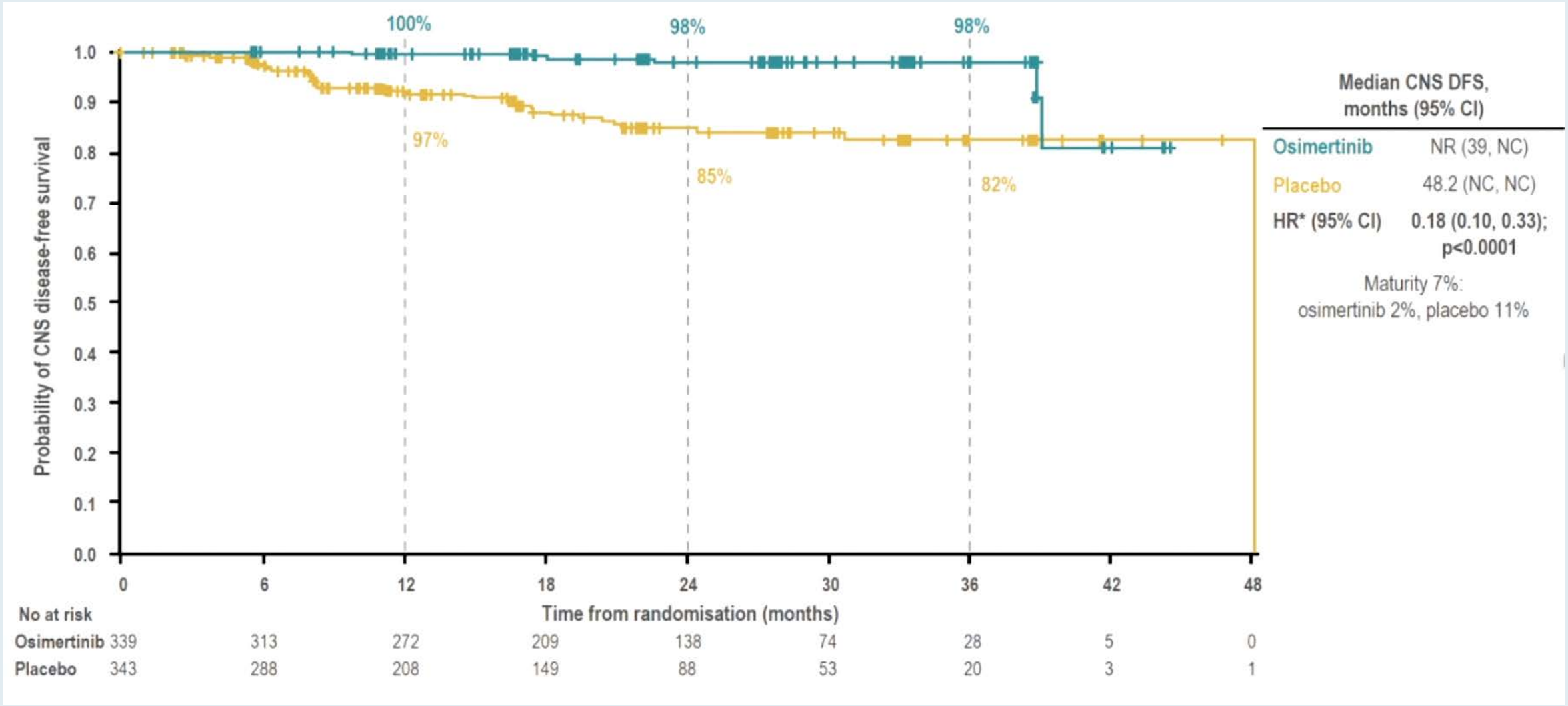
ADAURA: CNS DFS Events

- Overall, 45 patients (osimertinib n=6, placebo n=39) had CNS DFS events

	Overall population	
Patients, n (%)	**Osimertinib n=339**	**Placebo n=343**
CNS DFS events:	6 (2%)	39 (11%)
CNS recurrence	4 (1%)	33 (10%)
Death	2 (1%)	6 (2%)

Tsuboi M et al. ESMO 2020;Abstract LBA1.

ADAURA: CNS DFS in Overall Population



Tsuboi M et al. ESMO 2020;Abstract LBA1.

RTP RESEARCH TO PRACTICE

5-YEAR SURVIVAL OUTCOMES WITH DURVALUMAB AFTER CHEMORADIOTHERAPY IN UNRESECTABLE STAGE III NSCLC – AN UPDATE FROM THE PACIFIC TRIAL

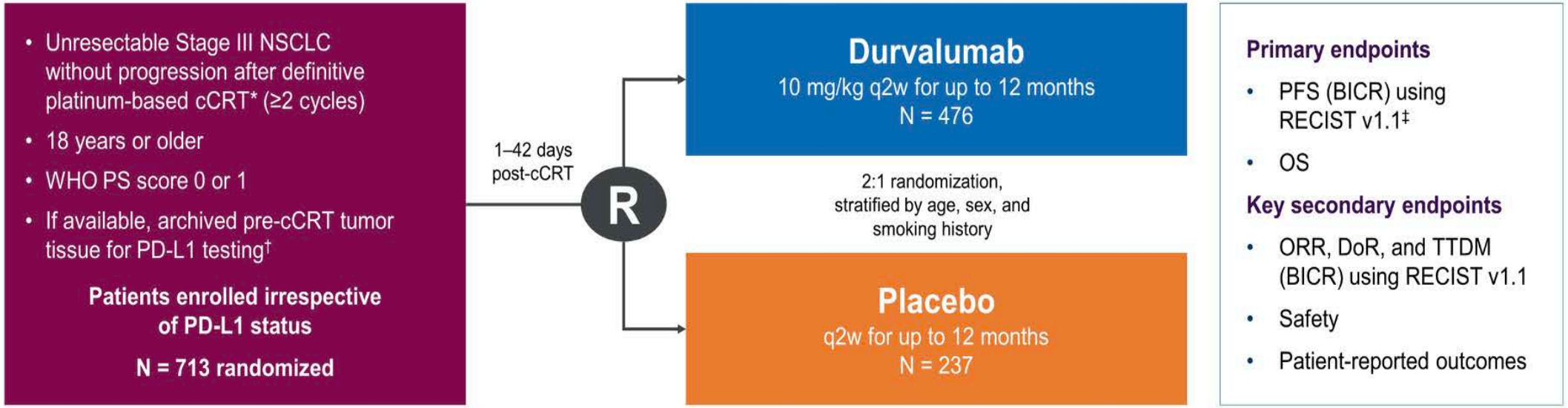
David R. Spigel,[1] Corinne Faivre-Finn,[2] Jhanelle E. Gray,[3] David Vicente,[4] David Planchard,[5] Luis Paz-Ares,[6] Johan F. Vansteenkiste,[7] Marina C. Garassino,[8,9] Rina Hui,[10] Xavier Quantin,[11] Andreas Rimner,[12] Yi-Long Wu,[13] Mustafa Özgüroğlu,[14] Ki H. Lee,[15] Terufumi Kato,[16] Maike de Wit,[17] Euan Macpherson,[18] Michael Newton,[19] Piruntha Thiyagarajah,[20] Scott J. Antonia[3]

[1]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, Tennessee, USA; [2]The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [3]H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA; [4]Hospital Universitario Virgen Macarena, Seville, Spain; [5]Department of Medical Oncology, Thoracic Unit, Gustave Roussy, Villejuif, France; [6]Universidad Complutense, CiberOnc, CNIO and Hospital Universitario 12 de Octubre, Madrid, Spain; [7]University Hospitals KU Leuven, Leuven, Belgium; [8]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [9]Department of Hematology/Oncology, The University of Chicago, Chicago, Illinois, USA; [10]Westmead Hospital and the University of Sydney, Sydney, NSW, Australia; [11]Montpellier Cancer Institute (ICM) and Montpellier Cancer Research Institute (IRCM), INSERM U1194, University of Montpellier, Montpellier, France; [12]Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, New York, USA; [13]Department of Pulmonary Oncology, Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China; [14]Istanbul University − Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; [15]Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Republic of Korea; [16]Kanagawa Cancer Center, Yokohama, Japan; [17]Vivantes Klinikum Neukölln, Berlin, Germany; [18]AstraZeneca, Macclesfield, UK; [19]AstraZeneca, Gaithersburg, MD, USA; [20]AstraZeneca, Cambridge, UK

June 4th, 2021

ASCO 2021;Abstract 8511

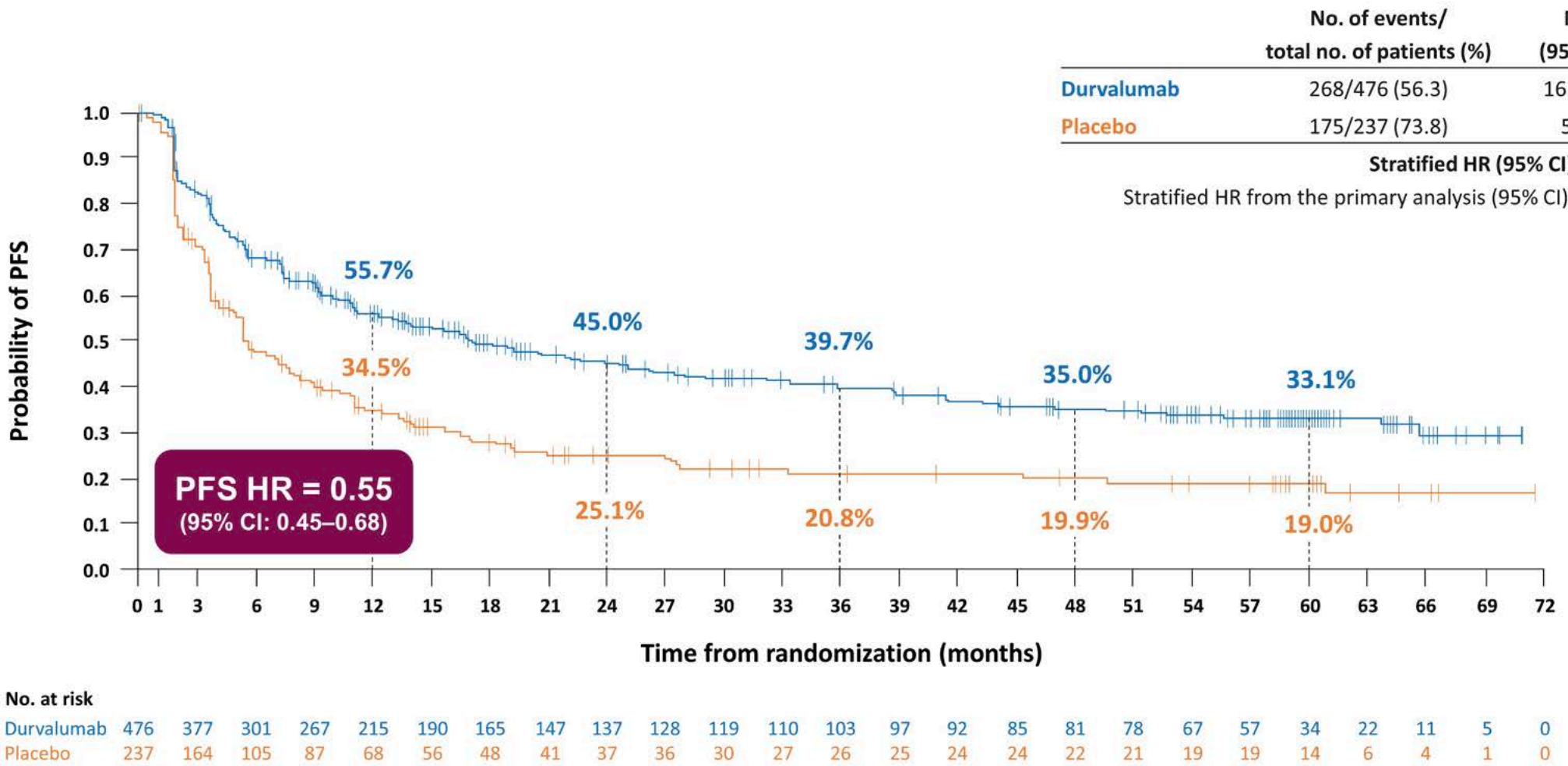
PACIFIC: Study Design



- **Updated analyses of OS and PFS, assessed ~5 years after the last patient was randomized (data cutoff: 11 January 2021; exploratory, post-hoc analysis)**
  - **Treatment effects were estimated using stratified log-rank tests in the ITT population**
  - **Medians and yearly landmark rates were estimated using the Kaplan–Meier method**

Spigel DR et al. ASCO 2021;Abstract 8511.

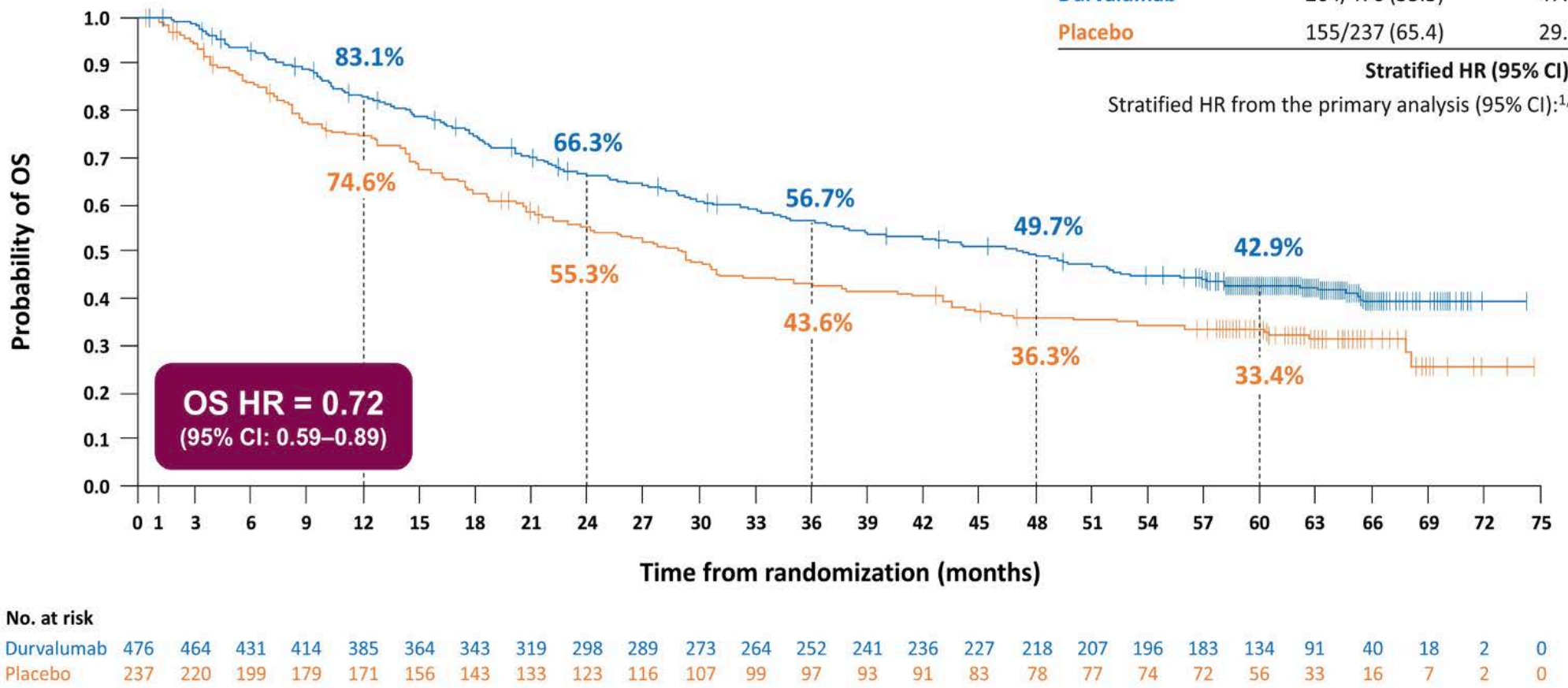
PACIFIC: Updated Progression-Free Survival (ITT)



Spigel DR et al. ASCO 2021;Abstract 8511.

RTP RESEARCH TO PRACTICE

PACIFIC: Updated Overall Survival (ITT)



	No. of events/ total no. of patients (%)	Median OS (95% CI), months
Durvalumab	264/476 (55.5)	47.5 (38.1–52.9)
Placebo	155/237 (65.4)	29.1 (22.1–35.1)

Stratified HR (95% CI): 0.72 (0.59–0.89)

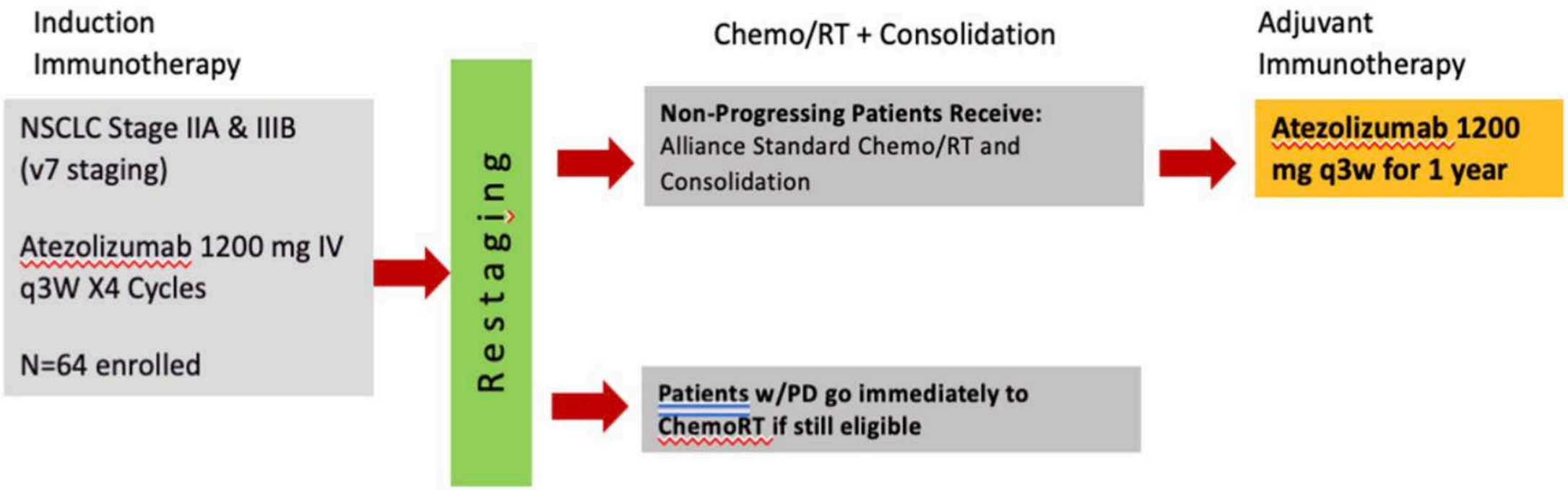
Stratified HR from the primary analysis (95% CI):[1,2] 0.68 (0.53–0.87)

No. at risk

Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

Spigel DR et al. ASCO 2021;Abstract 8511.

AFT-16 Phase II Trial



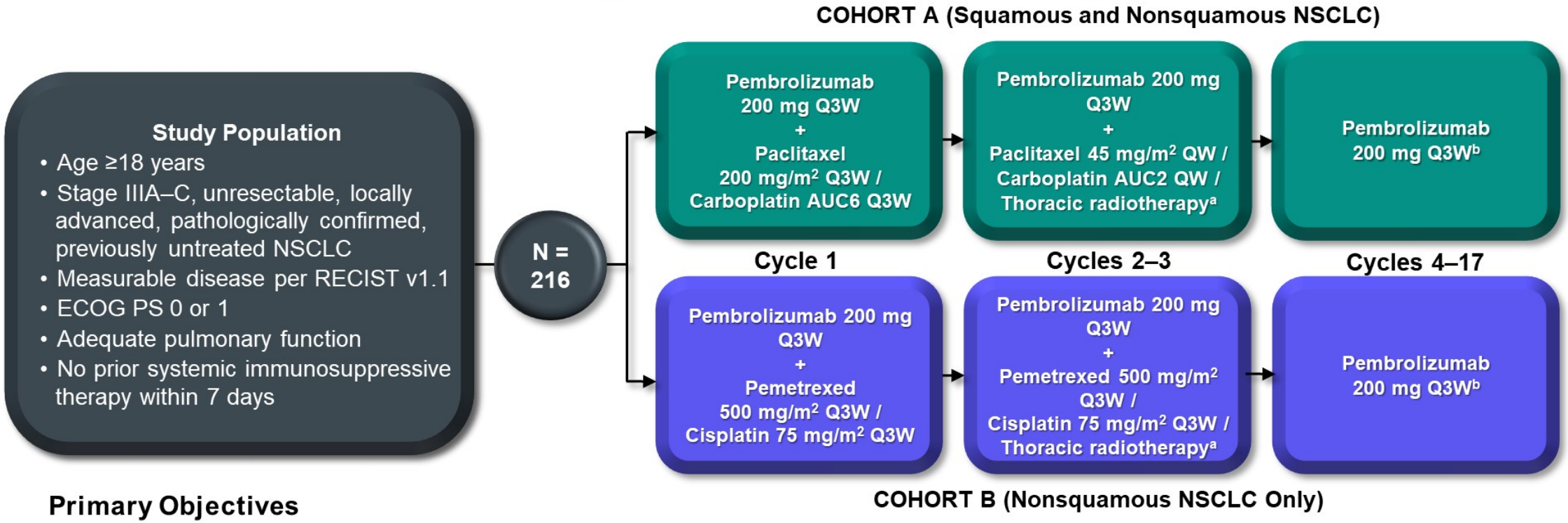
- Median PFS = 23.7 mo
- OS at 18 mo = 84%
- 1 pt each with Gr 3 pneumonitis/pneumonia/colitis, Gr 4 Guillain Barre
- PFS 12 and 18 mo from end CRT was 78% and 72% vs 56% and 44% in PACIFIC

Ross HJ, ASCO 2021; Abstract 8513.

Courtesy of Heather Wakelee, MD

KEYNOTE-799 Phase II Trial

KEYNOTE-799 (NCT03631784)



Primary Objectives

- ORR per RECIST v1.1 by BICR
- Patients who develop grade ≥3 pneumonitis

Secondary Objectives

- PFS per RECIST v1.1 by BICR, OS, safety

Statistical Analysis Details

- Efficacy and safety assessed in all patients as-treated

AUC, area under the concentration-time curve; BICR, blinded independent central review.
[a]60 Gy in 30 daily 2-Gy fractions. [b]Treatment continued until cycle 17 was completed or until documented disease progression, unacceptable AEs, intercurrent illness that prevents further administration of treatment, or study withdrawal. Pembrolizumab therapy was discontinued permanently in patients who develop grade ≥3 or recurrent grade 2 pneumonitis.

Jabbour SK et al. ASCO 2021;Abstract 8512

KEYNOTE-799

Efficacy Outcomes

Total Population	Cohort A (Squamous and Nonsquamous) n = 112		Cohort B (Nonsquamous) n = 102	
ORR, % (95% CI)	**70.5 (61.2–78.8)**		**70.6 (60.7–79.2)**	
CR	4 (3.6)		5 (4.9)	
PR	75 (67.0)		67 (65.7)	
SD	20 (17.9)		23 (22.5)	
PD	1 (0.9)		0	
Not evaluable[a]/No assessment[b]	2 (1.8) / 10 (8.9)		0 / 7 (6.9)	
DOR, median (range),[c] mo	NR (1.7+ to 19.7+)		NR (1.8+ to 21.4+)	
DOR ≥12 mo,[c] %	79.7		75.6	
PFS,[c] median (95% CI), mo	NR (16.6–NR)		NR (NR–NR)	
12-mo PFS rate, %	67.1		71.6	
OS,[c] median (95% CI), mo	NR (NR–NR)		NR (21.9–NR)	
12-mo OS rate, %	81.3		87.0	
PD-L1 Status	**TPS <1% (n = 21)**	**TPS ≥1% (n = 66)**	**TPS <1% (n = 28)**	**TPS ≥1% (n = 40)**
ORR, n (%)	14 (66.7)	50 (75.8)	20 (71.4)	29 (72.5)
Histology	**Nonsquamous (n = 39)**	**Squamous (n = 73)**	**Nonsquamous (n = 102)**	**Squamous (n = 0)**
ORR, n (%)	27 (69.2)	52 (71.2)	72 (70.6)	NA

DOR, duration of response; NR, not reached; TPS, tumor proportion score. "+" indicates no PD by the time of last disease assessment.
[a]Postbaseline assessment available but not evaluable or CR/PR/SD <6 weeks from first dose. [b]No postbaseline assessment available for response evaluation. [c]Kaplan-Meier estimate.
Data cutoff date: October 28, 2020.

Jabbour SK et al. ASCO 2021;Abstract 8512

First-in-Class Registrational Clinical Trial of Sugemalimab Met Its Primary Endpoint for Stage III NSCLC and Plans to Submit a New Drug Application

Press Release – May 28, 2021

"The registrational clinical trial (GEMSTONE-301 study) of the anti-PD-L1 monoclonal antibody sugemalimab in patients with stage III NSCLC met its primary endpoint at a planned interim analysis reviewed by the independent Data Monitoring Committee. The findings showed that sugemalimab as a consolidation therapy brought statistically significant and clinically meaningful improvement in the Blinded Independent Central Review assessed PFS in patients with locally advanced/unresectable NSCLC without disease progression after concurrent or sequential chemoradiotherapy. Investigator assessed PFS showed consistent results as those of the primary endpoint. Sugemalimab was well-tolerated with no new safety signals. Subgroup analyses demonstrated that sugemalimab was associated with clinical benefit regardless of whether patients received concurrent or sequential chemoradiotherapy prior to sugemalimab."

https://www.prnewswire.com/in/news-releases/cstone-announces-the-first-in-class-registrational-clinical-trial-of-sugemalimab-met-its-primary-endpoint-in-stage-iii-nsclc-and-plans-to-submit-a-new-drug-application-861921807.html

What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
11:00 AM – 12:30 PM ET

Faculty

Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD
Robert Svatek, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.