Meet The Professor

Current and Future Role of Immunotherapy in the Management of Lung Cancer

Jarushka Naidoo, MB BCH, MHS
Consultant Medical Oncologist
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Adjunct Assistant Professor of Oncology
Johns Hopkins University
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Commercial Support

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Dr Love — Disclosures

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Contracted Research	AstraZeneca Pharmaceuticals LP, Merck
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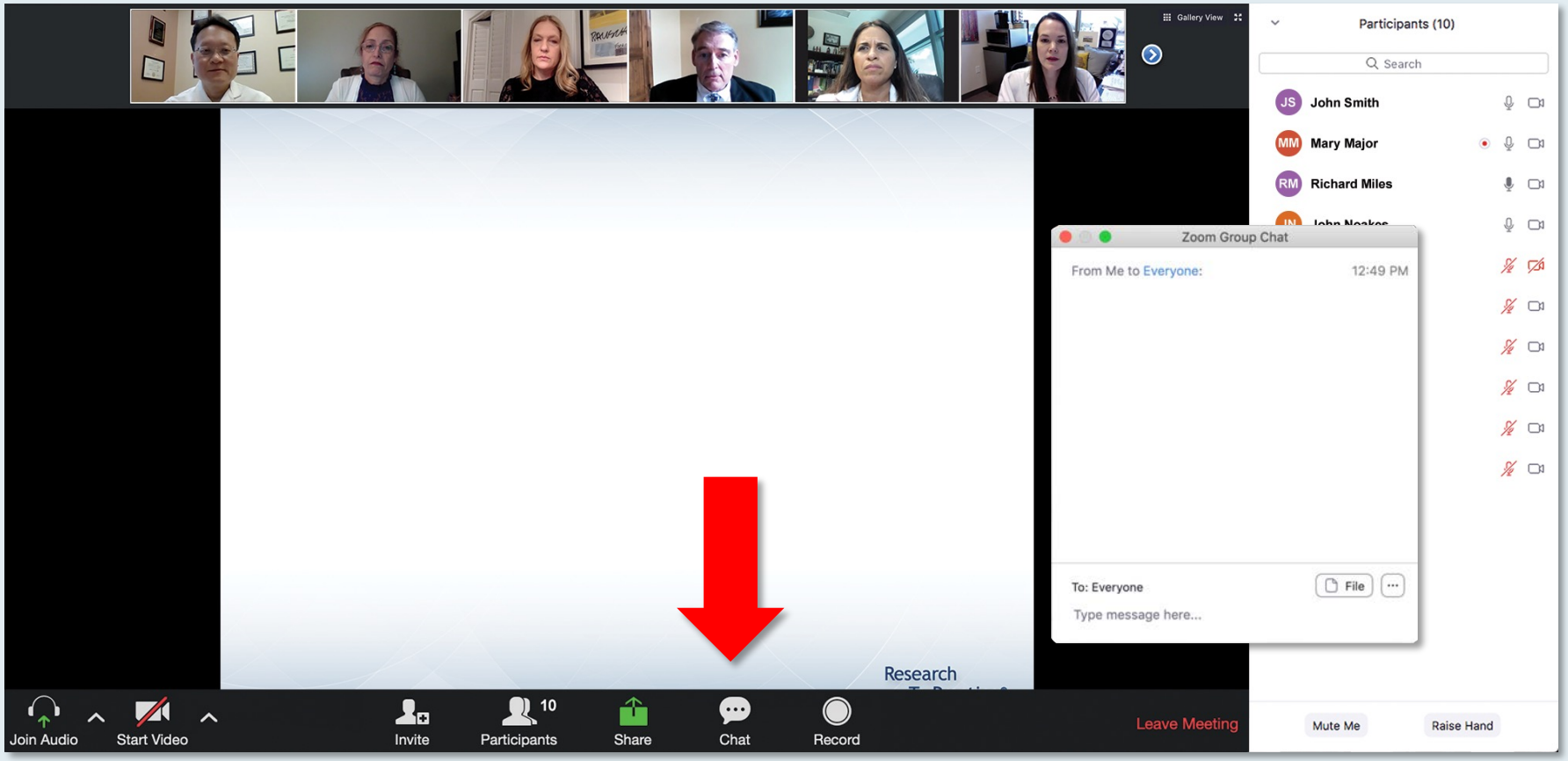
We Encourage Clinicians in Practice to Submit Questions



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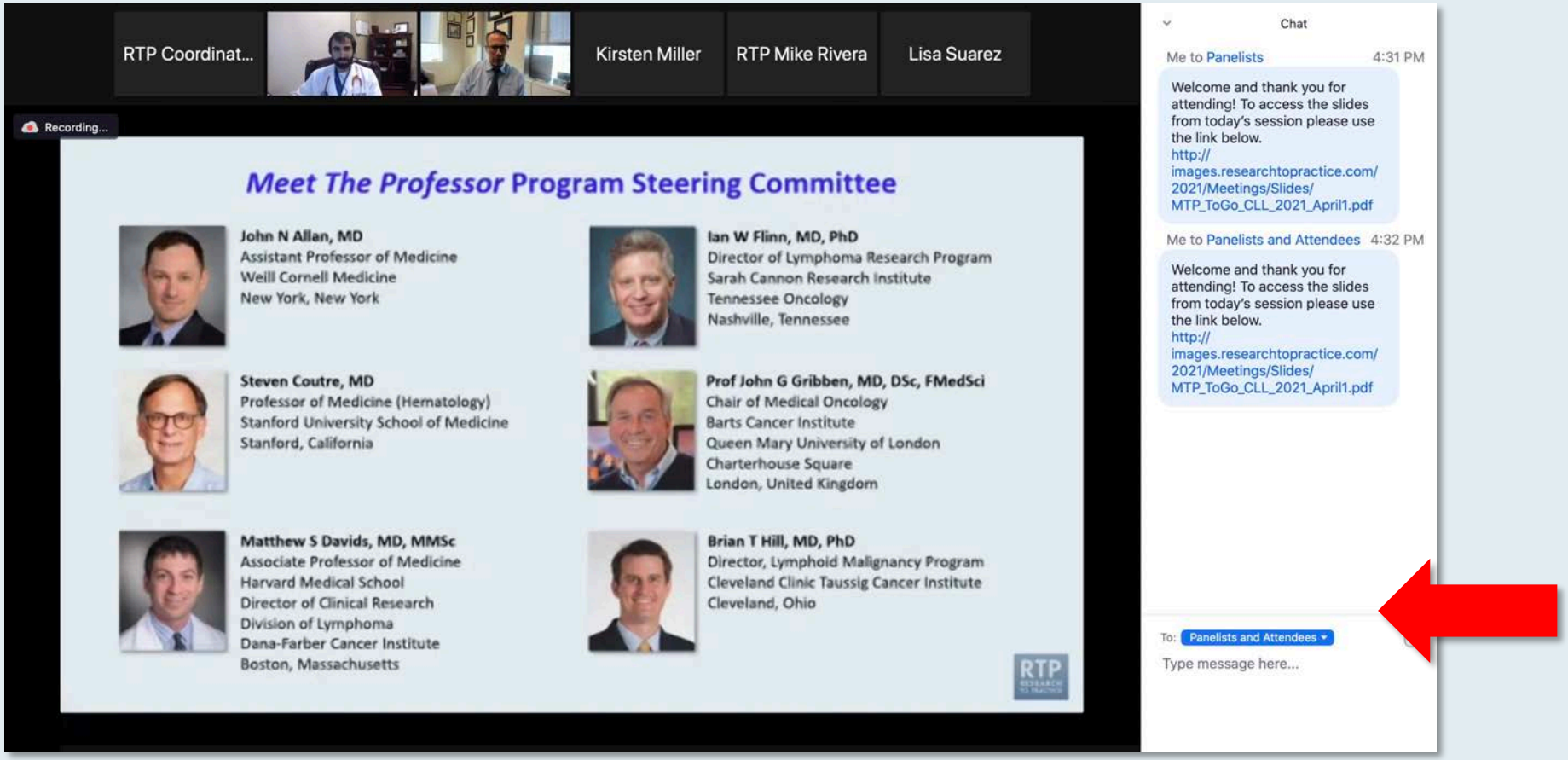
Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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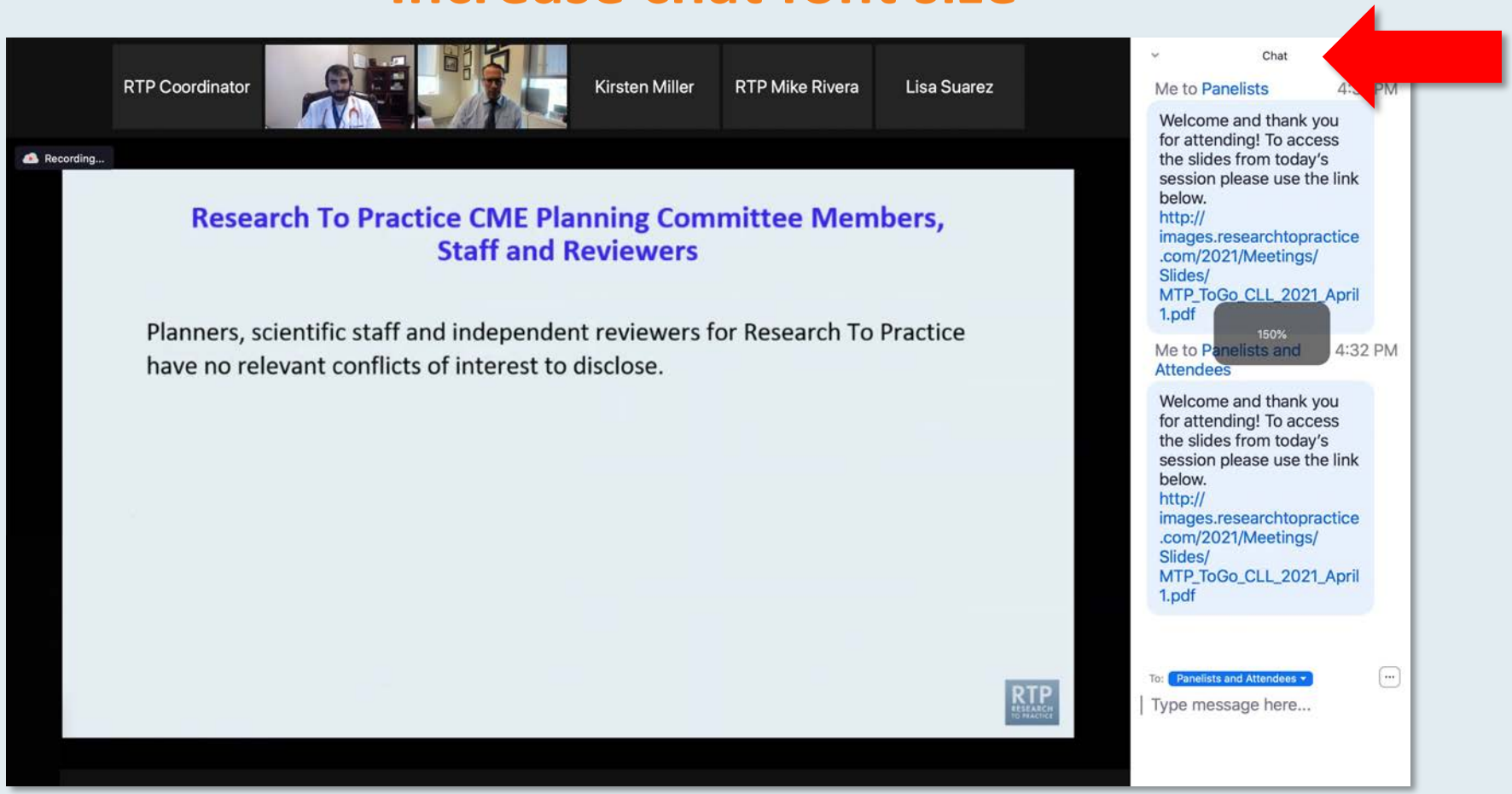

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

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Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Thursday, February 24, 2022
5:00 PM – 6:00 PM ET

Faculty
Amir Fathi, MD

Moderator
Neil Love, MD

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The Great Adjuvant Debate — Exploring the Role of Novel Therapies in the Management of Localized Cancer

Monday, February 28, 2022

5:00 PM – 6:00 PM ET

Faculty

Jeffrey S Weber, MD, PhD
Roy S Herbst, MD, PhD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Tuesday, March 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Michael E Williams, MD, ScM

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Wednesday, March 2, 2022
5:00 PM – 6:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 3, 2022
5:00 PM – 6:00 PM ET

Faculty

William G Wierda, MD, PhD

Moderator

Neil Love, MD

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Year in Review:
Kidney and Bladder Cancer

Tuesday, March 8, 2022
5:00 PM – 6:00 PM ET

Faculty

Elizabeth R Plimack, MD, MS
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

RTP Year in Review 2022

Thank you for joining us!

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

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Baltimore, Maryland

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Meet The Professor Program Participating Faculty

Charu Aggarwal, MD
Leslye M Heisler Associate Professor
for Lung Cancer Excellence
University of Pennsylvania
Abramson Cancer Center
Philadelphia, Pennsylvania

Sarah B Goldberg, MD, MPH
Associate Professor of Medicine
Medical Oncology
Yale School of Medicine
New Haven, Connecticut

Stephen V Liu, MD
Associate Professor of Medicine
Georgetown University Hospital
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Jarushka Naidoo, MB BCH, MHS
Consultant Medical Oncologist
Beaumont Hospital
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Adjunct Assistant Professor of Oncology
Johns Hopkins University
Baltimore, Maryland

MODERATOR
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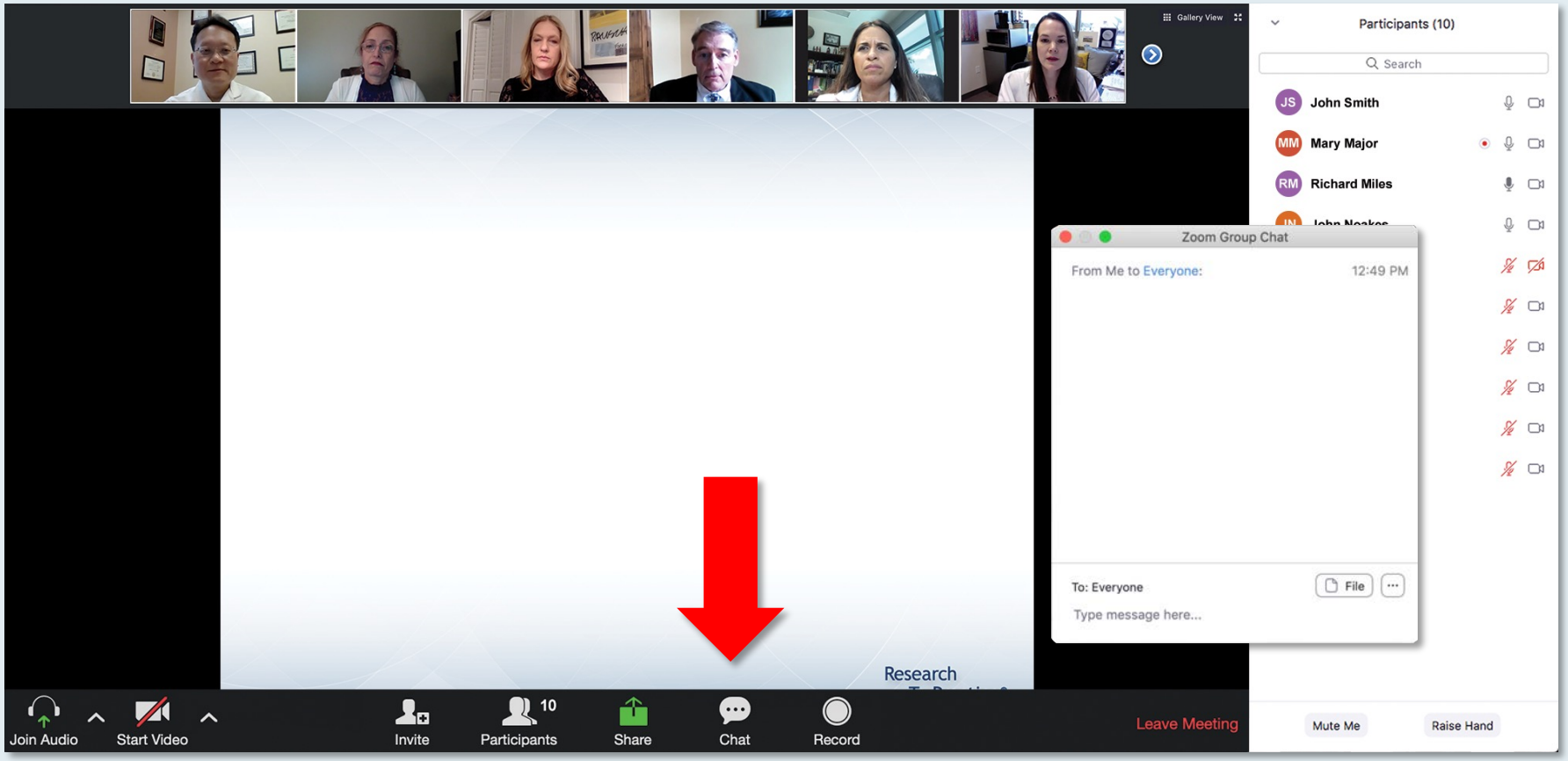
We Encourage Clinicians in Practice to Submit Questions



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ONCOLOGY TODAY

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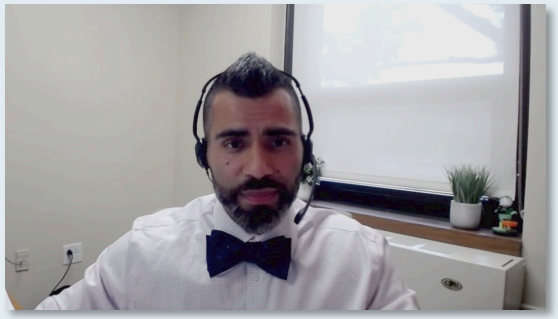
Sunil Gandhi, MD
Lecanto, Florida

Nikesh Jasani, MD
Houston, Texas



Rohit Gosain, MD
Jamestown, New York

Kapisthalam (KS) Kumar, MD
New Port Richey, Florida

Ranju Gupta, MD
Bethlehem, Pennsylvania

Raymond Lobins, DO
Mentor, Ohio

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Meet The Professor with Dr Naidoo

Introduction

MODULE 1: Adjuvant and Neoadjuvant Immunotherapy

MODULE 2: Consolidation Immunotherapy After Chemoradiation for Unresectable Locally Advanced Non-Small Cell Lung Cancer

MODULE 3: Immunotherapy for Metastatic Disease

MODULE 4: Special Considerations in Immunotherapy: Acute and Delayed Toxicity; Cure?

MODULE 5: Immunotherapy in Mesothelioma

MODULE 6: Immunotherapy and Novel Agents in Small Cell Lung Cancer

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Trastuzumab Deruxtecan Significantly Improved Both Progression-Free and Overall Survival in DESTINTY-Breast04 Trial for Patients with HER2-Low Metastatic Breast Cancer

Press Release: February 21, 2022

"Positive high-level results from the pivotal DESTINY-Breast04 Phase III trial showed fam-trastuzumab deruxtecan-nxki demonstrated a statistically significant and clinically meaningful improvement in both progression-free survival (PFS) and overall survival (OS) in patients with HER2-low unresectable and/or metastatic breast cancer regardless of hormone receptor (HR) status versus physician's choice of chemotherapy.

Up to 55% of all patients with breast cancer have tumors with an HER2 IHC score of 1+, or 2+ in combination with a negative ISH test, a level of HER2 expression not currently eligible for HER2-targeted therapy. HER2-low expression occurs in both HR-positive and HR-negative disease.

Currently, chemotherapy remains the only treatment option both for patients with HR-positive tumors following progression on endocrine (hormone) therapy, and for those who are HR-negative."

https://finance.yahoo.com/news/enhertu-fam-trastuzumab-deruxtecan-nxki-161500917.html

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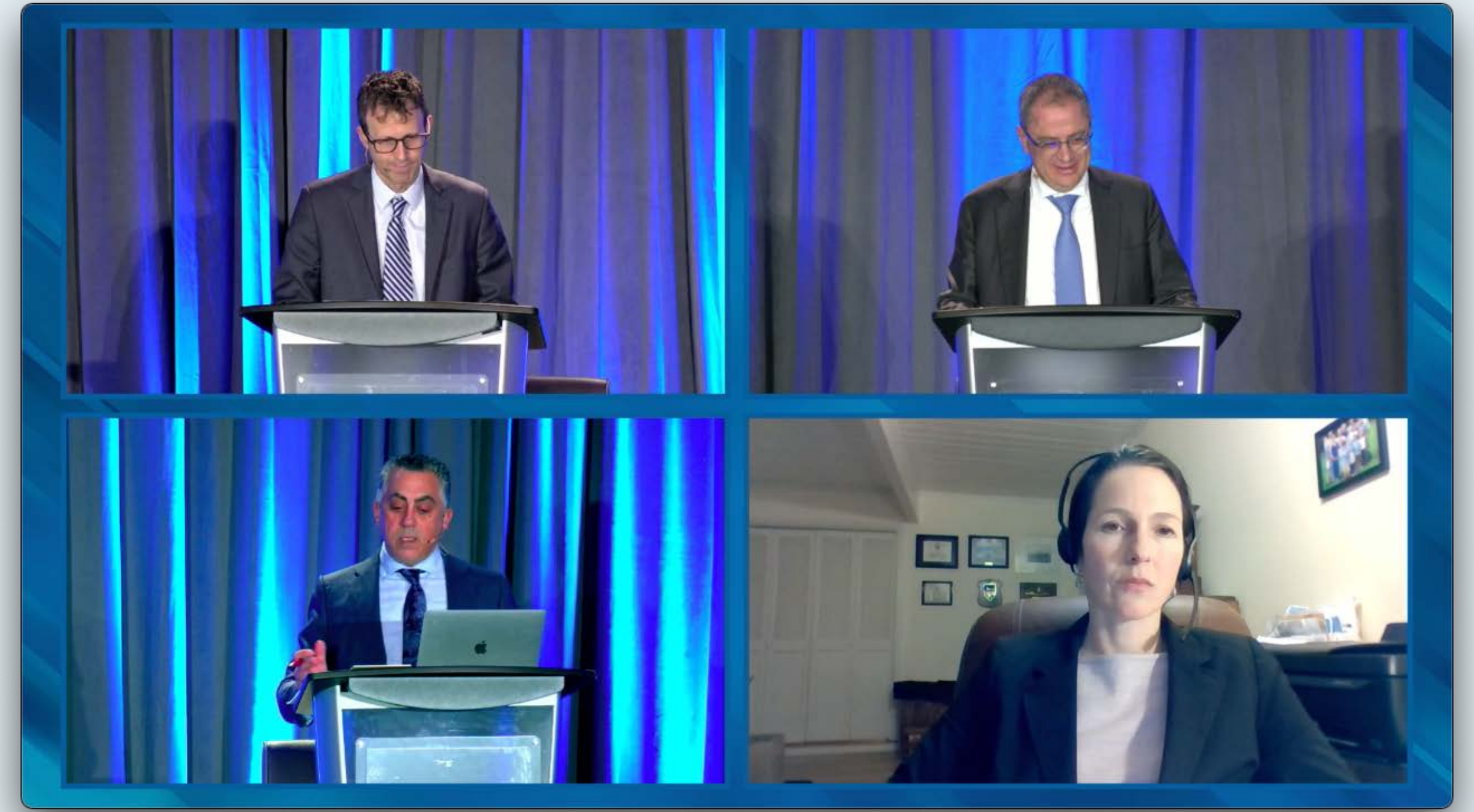

ASCO Gastrointestinal Cancers Symposium

Abstract 379

Fri, Jan 21, 2022

Phase 3 randomized, open-label, multicenter study of tremelimumab and durvalumab as first-line therapy in patients with unresectable hepatocellular carcinoma: HIMALAYA

Ghassan K Abou-Alfa,[1,2*] Stephen L Chan,[3*] Masatoshi Kudo,[4*] George Lau,[5*] Robin Kate Kelley,[6] Junji Furuse,[7] Wattana Sukeepaisarnjaroen,[8] Yoon-Koo Kang,[9] Tu V Dao,[10] Enrico N De Toni,[11] Lorenza Rimassa,[12,13] Valery Breder,[14] Alexander Vasilyev,[15] Alexandra Heurgué,[16] Vincent C Tam,[17] Kabir Mody,[18] Satheesh Chiradoni Thungappa,[19] Philip He,[20] Alejandra Negro,[20] and Bruno Sangro[21]

[1]Department of Medicine, Memorial Sloan Kettering Center, New York, NY, USA; [2]Weill Medical College, Cornell University, New York, NY, USA; [3]State Key Laboratory of Translational Oncology, Department of Clinical Oncology, Sir Yue-Kong Pao Center for Cancer, The Chinese University of Hong Kong, Hong Kong, China; [4]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan; [5]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong, China; [6]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA; [7]Department of Medical Oncology, Kyorin University Faculty of Medicine, Mitaka, Japan; [8]Department of Medicine, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand; [9]Department of Oncology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea; [10]Cancer Research and Clinical Trial Center, National Cancer Hospital, Hanoi, Vietnam; [11]Department of Medicine II, University Hospital, LMU Munich, Munich, Germany; [12]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy; [13]Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy; [14]Chemotherapy Department No17, N.N. Blokhin Russian Cancer Research Center, Moscow, Russia; [15]Railway Clinical Hospital, St. Petersburg, Russia; [16]Service d'Hépato-Gastro-entérologie, Hôpital Robert-Debré, Reims, France; [17]Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada; [18]Division of Hematology/Oncology, Department of Medicine, Mayo Clinic, Jacksonville, FL, USA; [19] Sri Venkateshwara Hospital, Bangalore, India; [20]AstraZeneca, Gaithersburg, MD, USA; [21]Liver Unit and HPB Oncology Area, Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain

*Drs Ghassan K Abou-Alfa, Stephen L Chan, Masatoshi Kudo, and George Lau contributed equally to this work.

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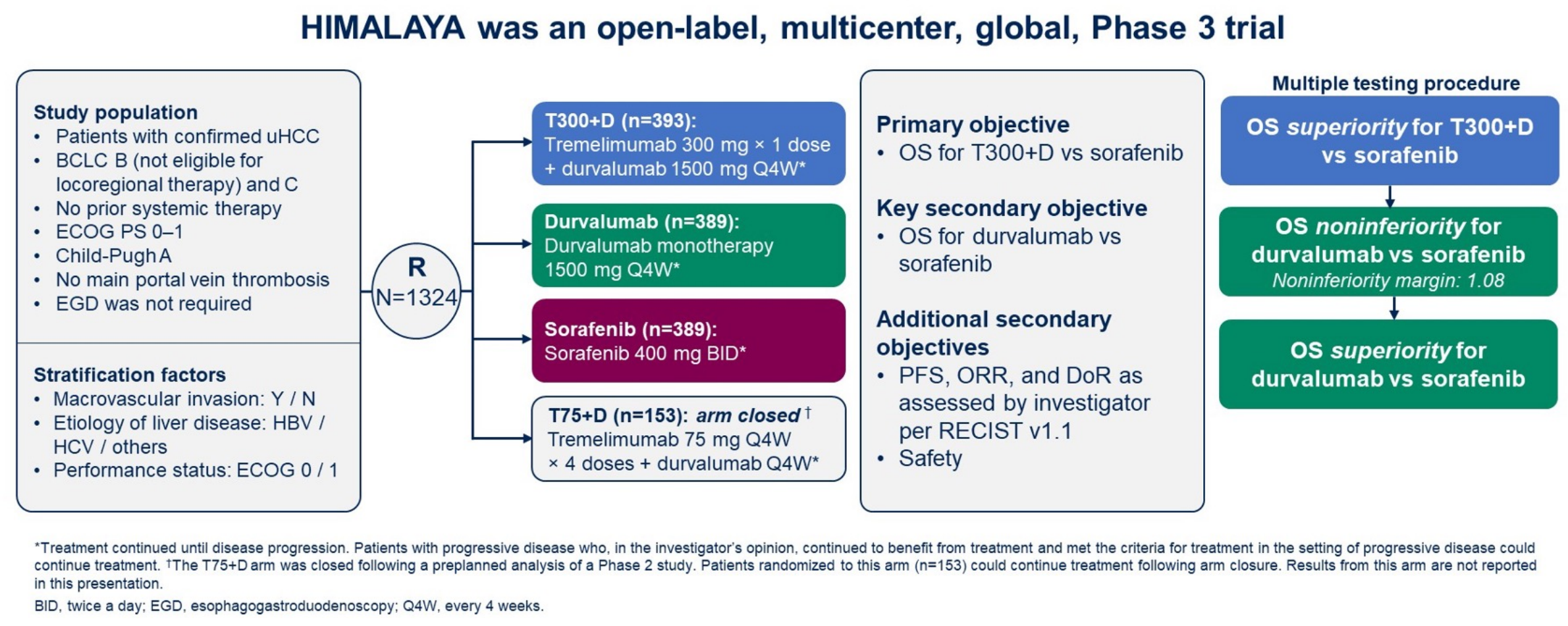
HIMALAYA Phase III Trial Schema



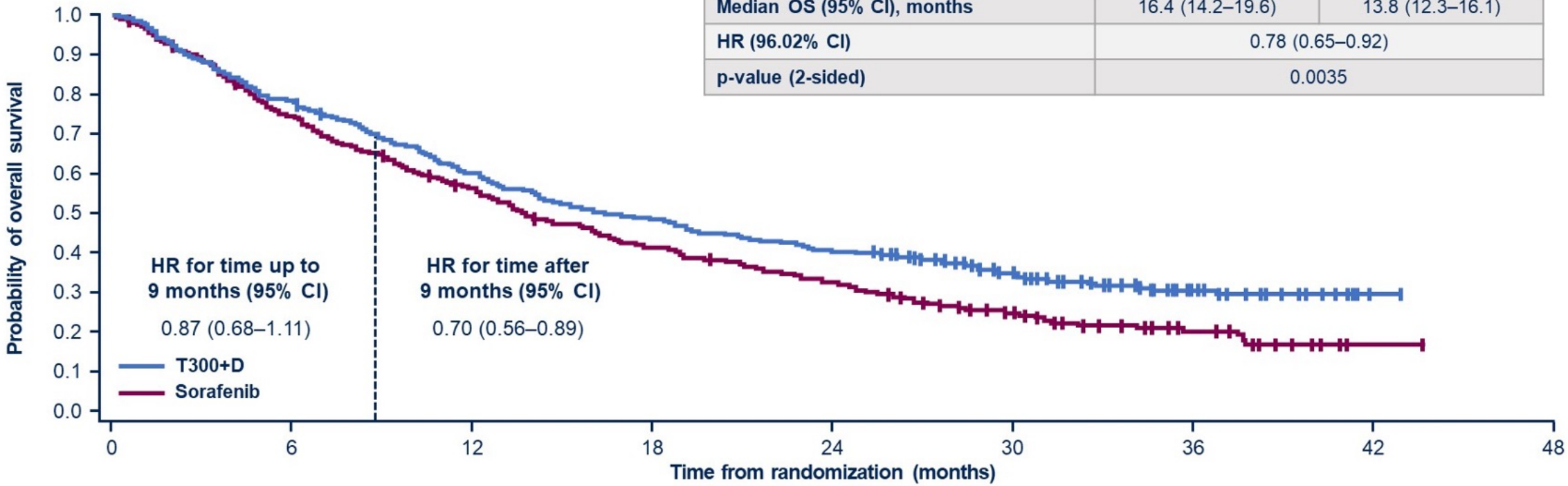
*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned analysis of a Phase 2 study. Patients randomized to this arm (n=153) could continue treatment following arm closure. Results from this arm are not reported in this presentation.

BID, twice a day; EGD, esophagogastroduodenoscopy; Q4W, every 4 weeks.

Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379. Friday, January 21, 2022.

HIMALAYA Primary Endpoint: OS for Tremelimumab 300 and Durvalumab as First-Line Therapy in Unresectable HCC

	T300+D (n=393)	Sorafenib (n=389)
OS events, n (%)	262 (66.7)	293 (75.3)
Median OS (95% CI), months	16.4 (14.2–19.6)	13.8 (12.3–16.1)
HR (96.02% CI)	0.78 (0.65–0.92)	
p-value (2-sided)	0.0035	



Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379. Friday, January 21, 2022.

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HIMALAYA: Safety and Tolerability

Event, n (%)	T300+D (n=388)	Durvalumab (n=388)	Sorafenib (n=374)
Any AE	378 (97.4)	345 (88.9)	357 (95.5)
Any TRAE*	294 (75.8)	202 (52.1)	317 (84.8)
Any grade 3/4 AE	196 (50.5)	144 (37.1)	196 (52.4)
Any grade 3/4 TRAE	100 (25.8)	50 (12.9)	138 (36.9)
Any serious TRAE	68 (17.5)	32 (8.2)	35 (9.4)
Any TRAE leading to death	9 (2.3)†	0	3 (0.8)‡
Any TRAE leading to discontinuation	32 (8.2)	16 (4.1)	41 (11.0)

Includes AEs with onset or increase in severity on or after the date of the first dose through 90 days following the date of the last dose or the date of initiation of the first subsequent therapy.

*Treatment-related was as assessed by investigator. †Nervous system disorder (n=1), acute respiratory distress syndrome (n=1), hepatitis (n=1), myocarditis (n=1), immune-mediated hepatitis (n=2), pneumonitis (n=1), hepatic failure (n=1), myasthenia gravis (n=1). ‡Hematuria (n=1), cerebral hematoma (n=1), hepatic failure (n=1).

AE, adverse event; SMQ, Standardized MedDRA Query; T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W; TRAE, treatment-related adverse event.

Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379. Friday, January 21, 2022.

Meet The Professor with Dr Naidoo

Introduction

MODULE 1: Adjuvant and Neoadjuvant Immunotherapy

- Dr Gupta: A 70-year-old woman with Stage IIIB adenocarcinoma of the lung and no targetable mutations – PD-L1 22C3 TPS = 1%, intensity 2+; PD-L1 SP 142 TPS = 5%, intensity 3+

MODULE 2: Consolidation Immunotherapy After Chemoradiation for Unresectable Locally Advanced Non-Small Cell Lung Cancer

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Case Presentation: A 70-year-old woman with Stage IIIB adenocarcinoma of the lung and no targetable mutations – PD-L1 22C3 TPS = 1%, intensity 2+; PD-L1 SP 142 TPS = 5%, intensity 3+

Dr Ranju Gupta (Bethlehem, Pennsylvania)

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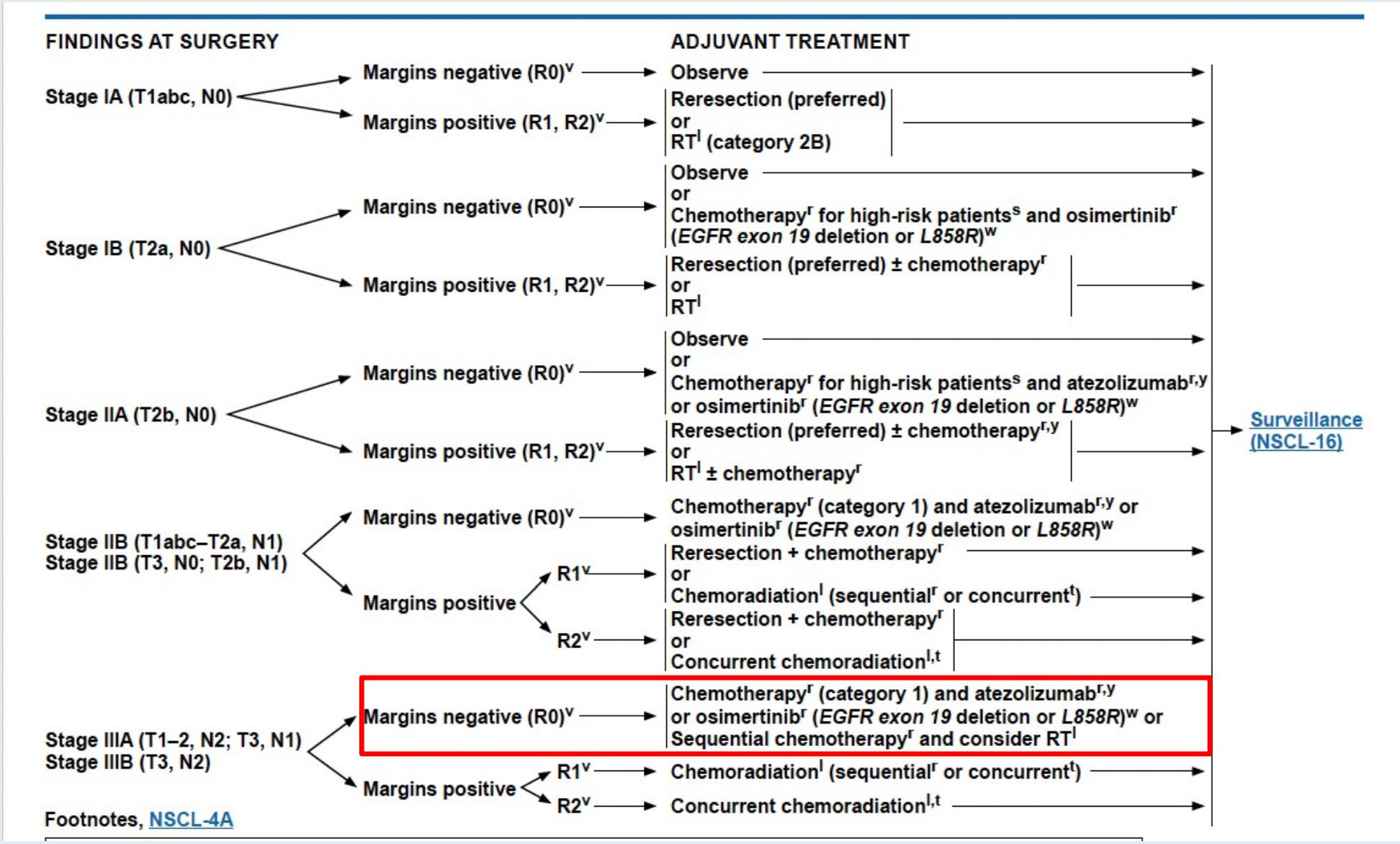
NCCN Guidelines Version 1.2022 NSCLC



NCCN Guidelines, Non-Small Cell Lung Cancer v1.2022.

In what situations, if any, are you currently recommending neoadjuvant chemotherapy (with or without an anti-PD-1/PD-L1 antibody) for your patients with non-small cell lung cancer (NSCLC)?

 Dr Aggarwal	None	 Dr Hanna	None
 Dr Goldberg	Select patients with Stage III disease	 Dr Liu	Resectable N2+ disease
 Dr Govindan	N2 disease with adequate pulmonary reserve	 Dr Ramalingam	Resectable N2 disease

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Based on available data and your clinical experience, does neoadjuvant immunotherapy (alone or with chemotherapy) increase the risk of surgical complications in patients with NSCLC?

 Dr Aggarwal	No	 Dr Hanna	No
 Dr Goldberg	No	 Dr Liu	No
 Dr Govindan	No	 Dr Ramalingam	It is too early to tell

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What are the advantages and disadvantages of neoadjuvant versus adjuvant immunotherapy?

Is there a role for a postneoadjuvant "KATHERINE" strategy in NSCLC?

Why did less than half of the patients in the control arm of IMpower010 receive immunotherapy (real world)?

Do patients who receive adjuvant atezolizumab respond to immunotherapy on disease relapse?

How often are delayed effects of immunotherapy observed?

What is the optimal duration of immunotherapy?

Is there likely a future role for MRD cell-free DNA assays and adjuvant and neoadjuvant therapy?

Reimbursement issues aside, would you offer adjuvant atezolizumab…

after chemotherapy to a patient with a PD-L1 of 1% to 49%?

without chemotherapy to a patient with a PD-L1 >50%?

after chemotherapy to a patient with a PD-L1 >50% and Stage IB cancer?

without chemotherapy to a patient with a PD-L1 >50% and Stage IB cancer?

without chemotherapy to a patient with a PD-L1 >50% and Stage IA cancer?

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Lancet 2021;398:1344-57

Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB–IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial

*Enriqueta Felip, Nasser Altorki, Caicun Zhou, Tibor Csőszi, Ihor Vynnychenko, Oleksandr Goloborodko, Alexander Luft, Andrey Akopov, Alex Martinez-Marti, Hirotsugu Kenmotsu, Yuh-Min Chen, Antonio Chella, Shunichi Sugawara, David Voong, Fan Wu, Jing Yi, Yu Deng, Mark McCleland, Elizabeth Bennett, Barbara Gitlitz, Heather Wakelee, for the IMpower010 Investigators**

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Contents lists available at ScienceDirect

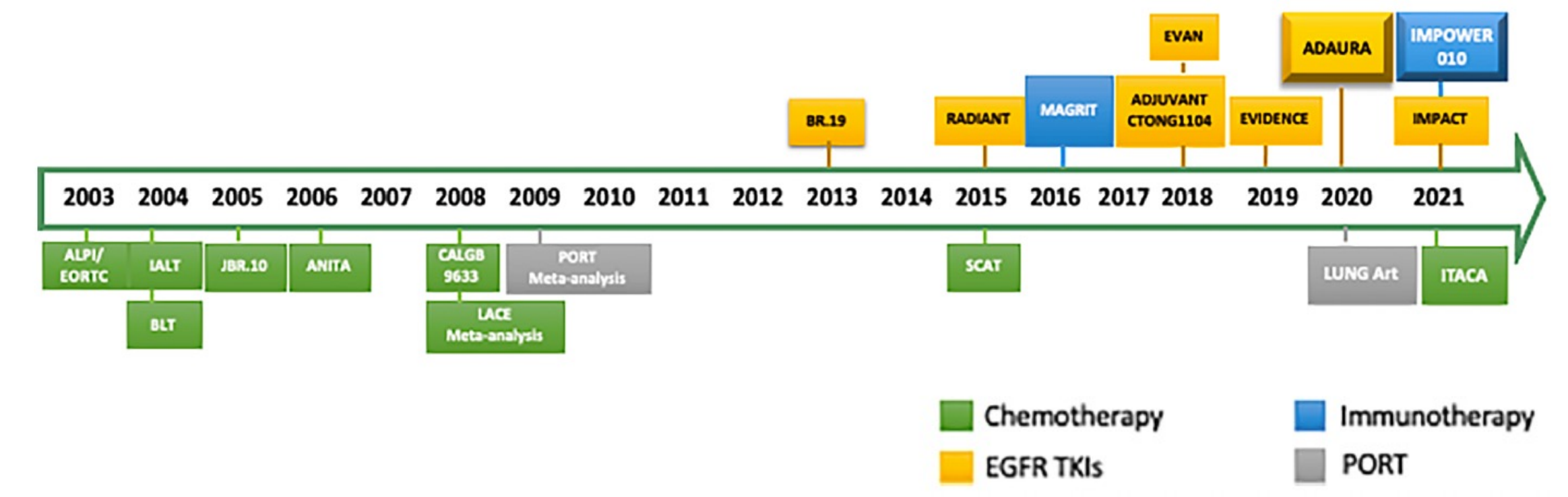
Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

Major breakthroughs in lung cancer adjuvant treatment: Looking beyond the horizon

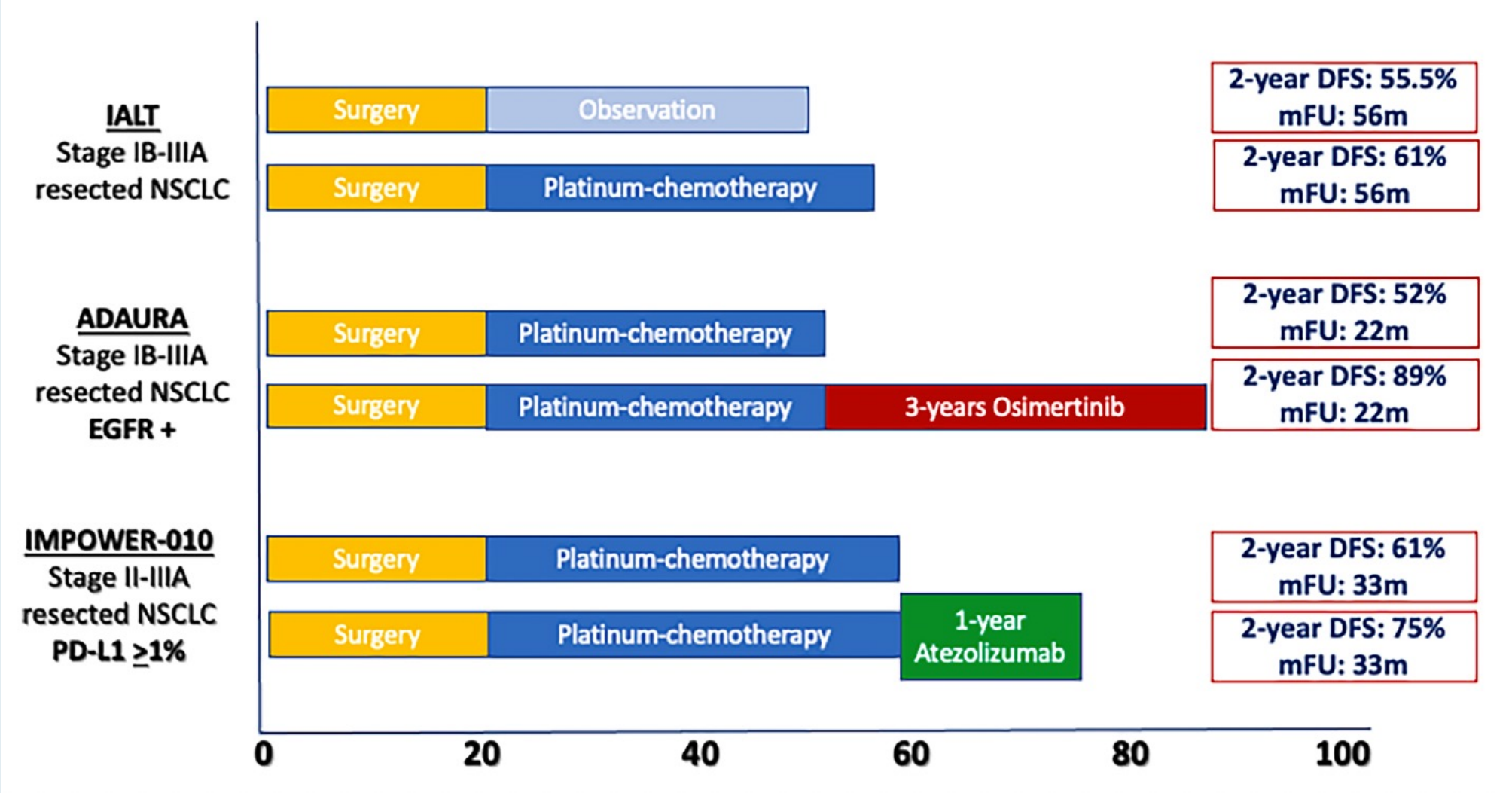
Francesco Passiglia [1], Valentina Bertaglia [1], Maria Lucia Reale [1], Marco Donatello Delcuratolo, Fabrizio Tabbò, Emanuela Olmetto, Enrica Capelletto, Paolo Bironzo, Silvia Novello [*]

Timeline of Adjuvant Clinical Trials for Surgically Resected NSCLC



Passiglia F et al. *Cancer Treat Rev* 2021;1010:102308.

Adjuvant Treatment Strategies for Surgically Resected NSCLC



Passiglia F et al. *Cancer Treat Rev* 2021;1010:102308.

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]

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IASLC 2021 World Conference on Lung Cancer
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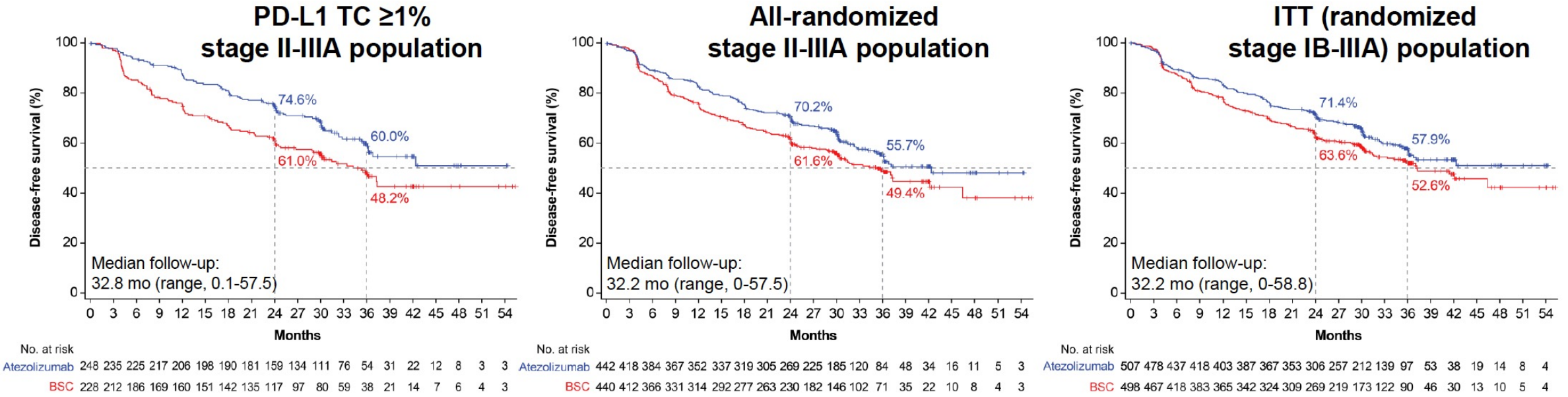
Abstract PL0205

DFS in the PD-L1 TC ≥1%[a] stage II-IIIA, all-randomized stage II-IIIA and ITT populations (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)	
P value[b]	0.004[c]	

	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[b]	0.02[c]	

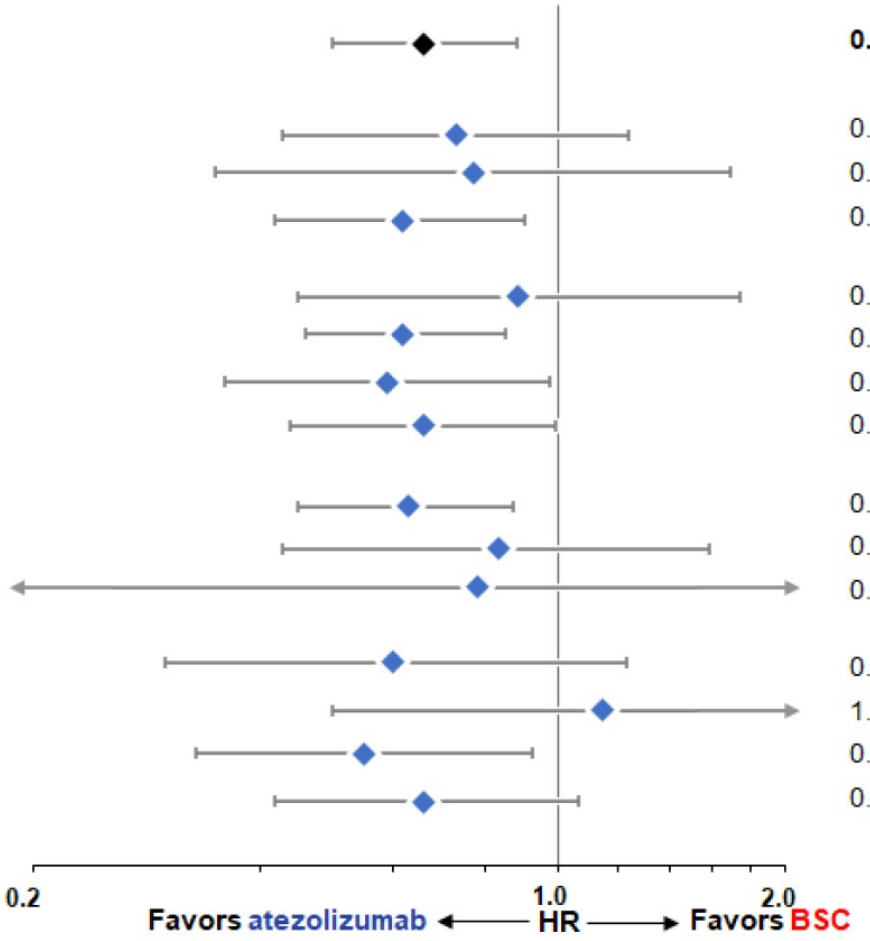
	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[b]	0.04[d]	

Clinical cutoff: January 21, 2021. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS. [d] The statistical significance boundary for DFS was not crossed.

Altorki N et al. World Conference on Lung Cancer 2021;Abstract PL0205.

PD-L1 TC ≥1%[a] 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. World Conference on Lung Cancer 2021;Abstract PL0205.

Conclusions

- At the DFS interim analysis of IMpower010, atezolizumab showed statistically significant DFS benefit vs BSC in the PD-L1 TC ≥1% stage II-IIIA (HR, 0.66; 95% CI: 0.50, 0.88) and all-randomized stage II-IIIA (HR, 0.79; 95% CI: 0.64, 0.96) populations
- The main reasons patients were not randomized after enrollment were patient withdrawal and disease progression
- In the ITT population:
  - Study arms were well balanced with regard to disease stage, regional lymph node status, surgical intervention and chemotherapy regimen
  - The majority of patients had lobectomy, lymph node dissection and 4 cycles of adjuvant chemotherapy
  - The median time from surgery to start of randomized treatment or BSC was similar between study arms
- In this exploratory analysis, improved DFS was observed with adjuvant atezolizumab vs BSC in the PD-L1 TC ≥1% stage II-IIIA and all-randomized stage II-IIIA populations – across most disease stages, in patients with nodal involvement, and across most surgery types and chemotherapy regimens

Altorki N et al. World Conference on Lung Cancer 2021;Abstract PL0205.

2021 ESMO congress

IMpower010: Sites of Relapse and Subsequent Therapy From a Phase 3 Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA NSCLC

Enriqueta Felip,[1] Eric Vallieres,[2] Caicun Zhou,[3] Heather Wakelee,[4] Igor Bondarenko,[5] Hiroshi Sakai,[6] Haruhiro Saito,[7] Grygorii Ursol,[8] Koji Kawaguchi,[9] Yunpeng Liu,[10] Evgeny Levchenko,[11] Nikolay Kislov,[12] Martin Reck,[13] Rüdiger Liersch,[14] Virginia McNally,[15] Qian Zhu,[16] Beiying Ding,[16] Elizabeth Bennett,[16] Barbara Gitlitz,[16] Nasser Altorki[17]

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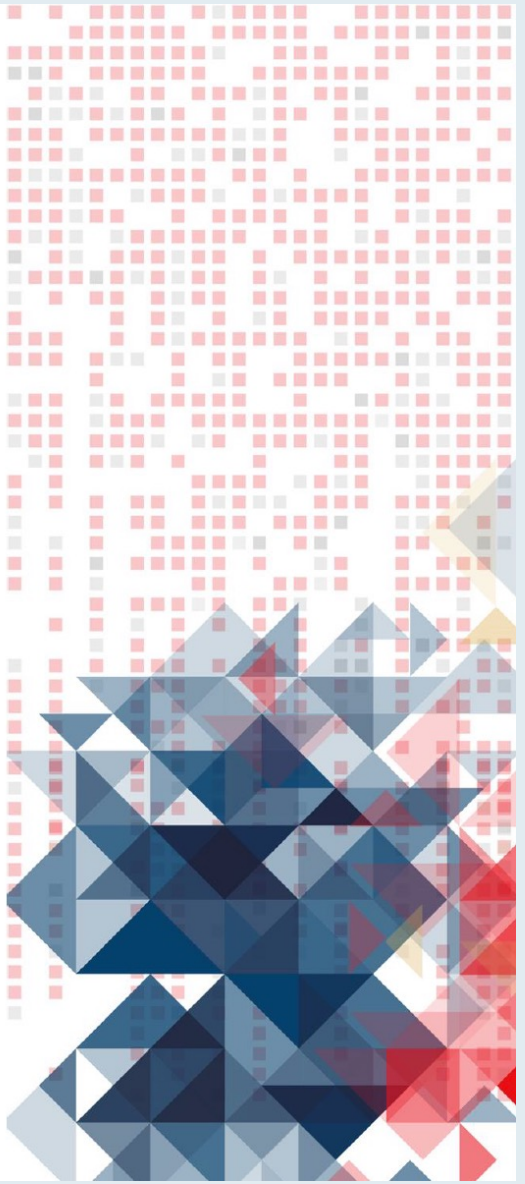

Abstract LBA9

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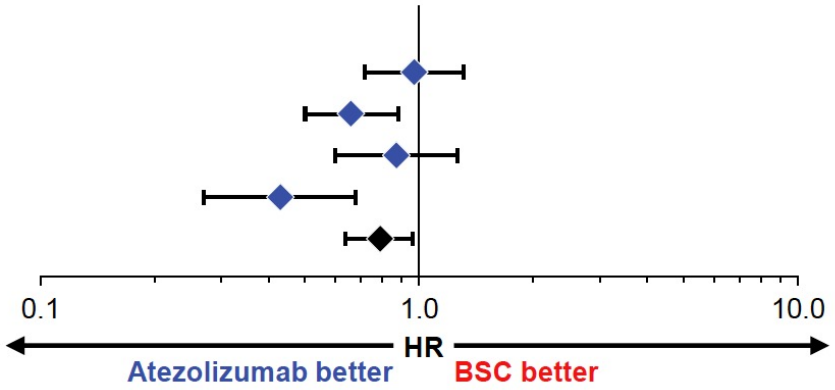
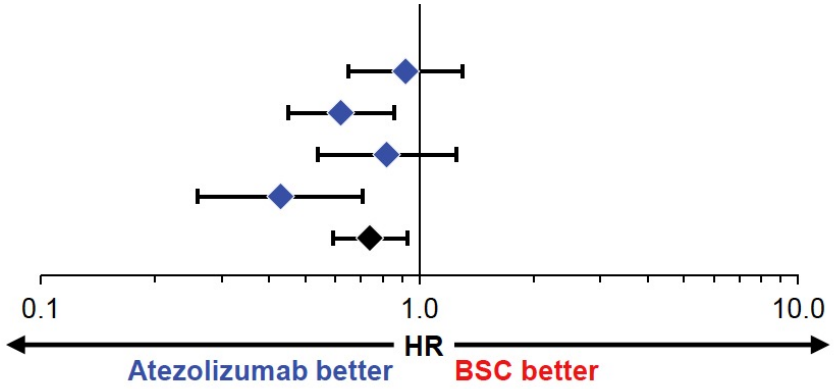
DFS by PD-L1 status[a]

All-randomised stage II-IIIA population (with and without known EGFR/ALK+ disease)

Subgroup *(including EGFR/ALK+)*	n	HR (95% CI)[b,c]
PD-L1 status by SP263		
TC <1%	383	0.97 (0.72, 1.31)
TC ≥1%	476	0.66 (0.50, 0.88)
TC 1-49%	247	0.87 (0.60, 1.26)
TC ≥50%	229	0.43 (0.27, 0.68)
All patients[d]	882	0.79 (0.64, 0.96)



Subgroup *(excluding EGFR/ALK+)*[e]	n	HR (95% CI)[f,g]
PD-L1 status by SP263		
TC <1%	312	0.92 (0.65, 1.30)
TC ≥1%	410	0.62 (0.45, 0.86)
TC 1-49%	201	0.82 (0.54, 1.25)
TC ≥50%	209	0.43 (0.26, 0.71)
All patients[h]	743	0.74 (0.59, 0.93)

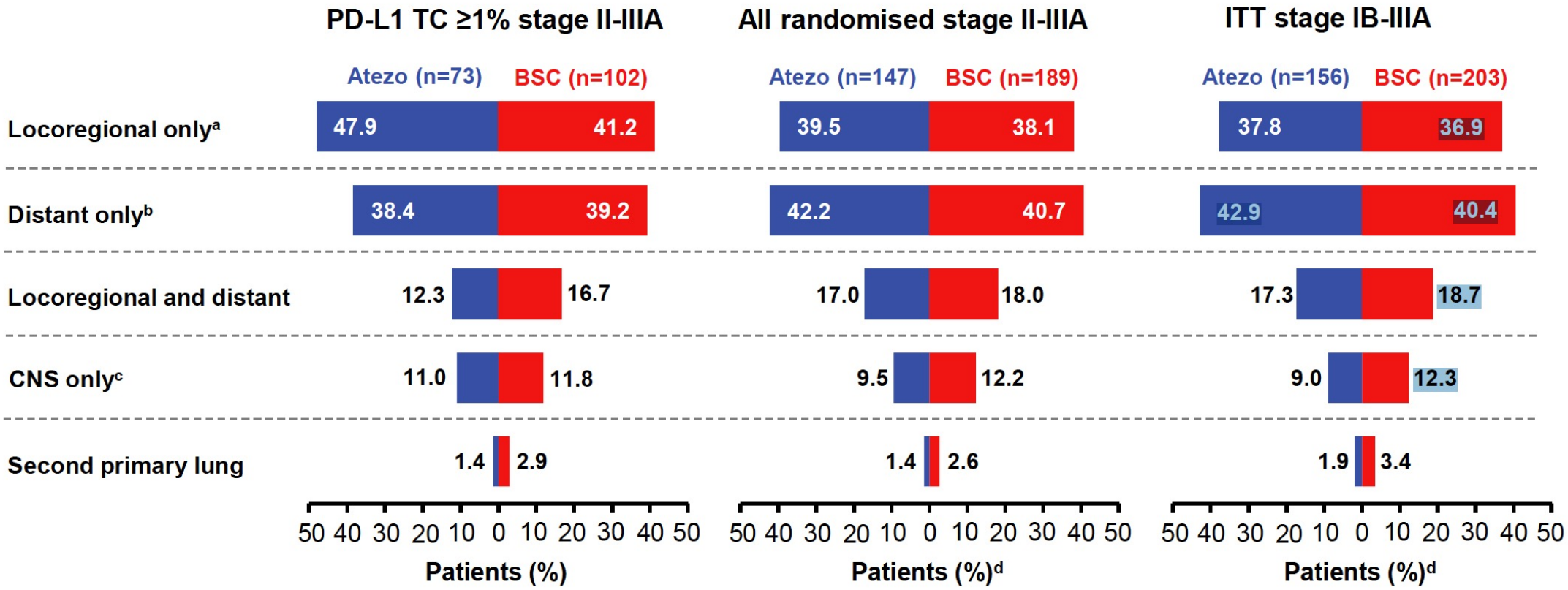


Clinical cutoff: 21 January 2021. [a] Per SP263 assay.
[b] Stratified for all patients and PD-L1 TC ≥1%; unstratified for all other subgroups. [c] DFS analyses in the PD-L1 TC <1% and TC 1-49% subgroups were exploratory. [d] 23 patients had unknown PD-L1 status as assessed by SP263. [e] Excluding patients with known *EGFR/ALK*+ NSCLC. [f] Unstratified for all subgroups. [g] EGFR/ALK+ exclusion analyses were post hoc. [h] 21 patients had unknown PD-L1 status as assessed by SP263.

Felip et al. IMpower010 Relapse Patterns. https://bit.ly/3mNMSAi

Felip E et al. ESMO 2021;Abstract LBA9.

Patterns of relapse



Clinical cutoff: 21 January 2021. [a] Includes patients with 'local' and/or 'regional' recurrence only. [b] Includes patients with distant sites only; patients could have >1 distant site. [c] Subset of the Distant only category; includes patients with only distant CNS site. Patients with recurrence in CNS and other sites are not included. [d] One patient in the BSC arm had distant + second primary non-lung sites.

Felip et al. IMpower010 Relapse Patterns. https://bit.ly/3mNMSAi

Felip E et al. ESMO 2021;Abstract LBA9.

Summary

- IMpower010 is the first positive Phase III study of adjuvant CIT after surgical resection and adjuvant chemotherapy in patients with early-stage NSCLC, showing a 34% reduction in risk of disease recurrence or death with adjuvant atezolizumab in the PD-L1 TC ≥1% stage II-IIIA population (HR, 0.66; 95% CI: 0.50, 0.88) and potentially changing the standard of care in this population
  - In an exploratory analysis of the PD-L1 TC 1-49% population, the DFS HR was 0.87 (95% CI: 0.60, 1.26)
  - The greatest magnitude of DFS benefit was observed in the PD-L1 TC ≥50% population (HR, 0.43; 95% CI: 0.27, 0.68; secondary endpoint)
  - In a post-hoc analysis excluding patients with known *EGFR/ALK*+ NSCLC, DFS HRs were numerically improved in most PD-L1 subgroups
- At this DFS interim analysis, similar patterns of relapse were seen between the study arms
- Time to relapse appeared to favour the atezolizumab vs BSC arm in the PD-L1 TC ≥1% stage II-IIIA population, with minimal differences seen in the all-randomised stage II-IIIA and ITT populations
- A higher rate of post-relapse CIT use was observed in the BSC arm
- Longer term follow-up is warranted and may reveal differences in relapse patterns and treatment options

CIT = chemoimmunotherapy

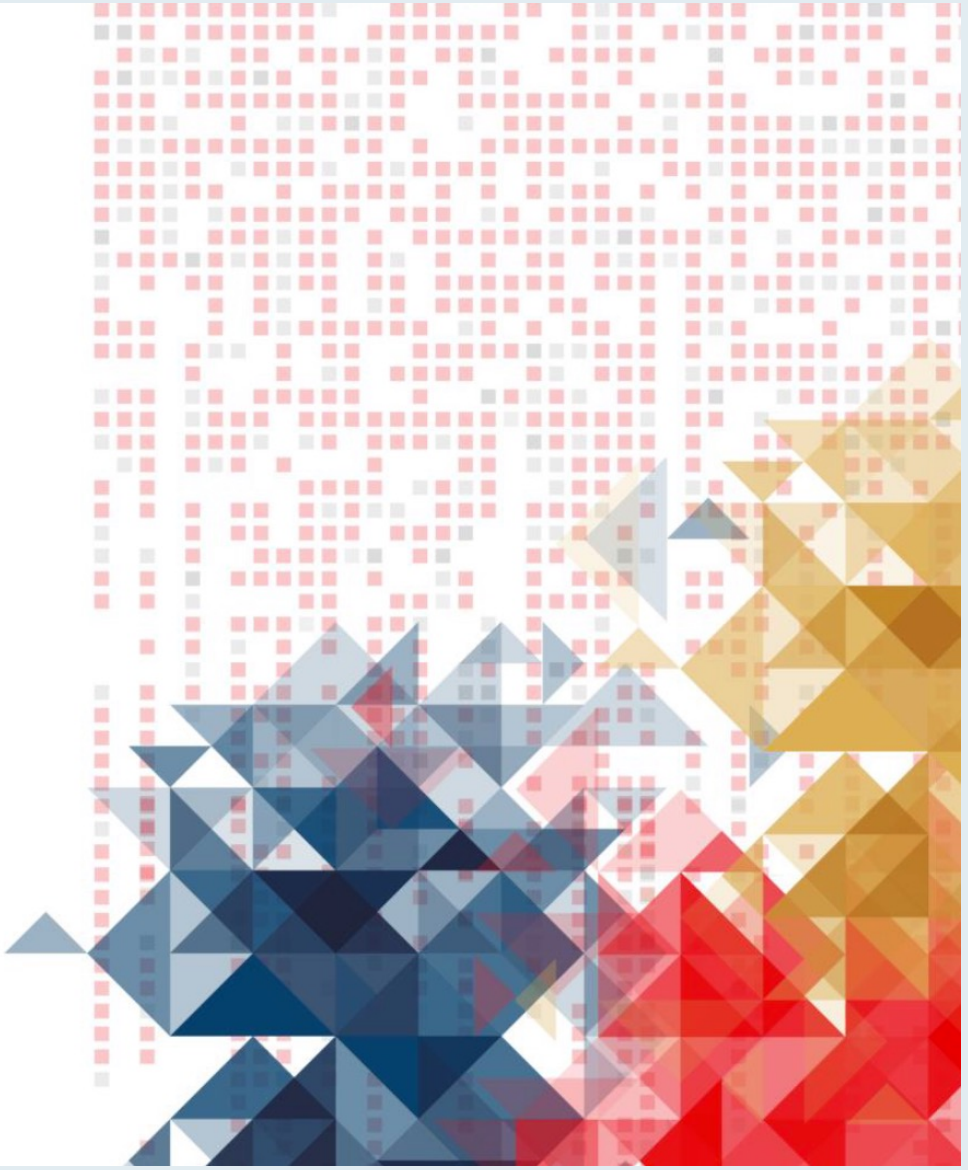
Felip E et al. ESMO 2021;Abstract LBA9.

2021 ESMO congress

IMPOWER 010
« Jamais 2 sans 3 »

Prof. Benjamin Besse

Head of Clinical Research, Gustave Roussy, France
Chair of the Scientific Chairs Council, EORTC



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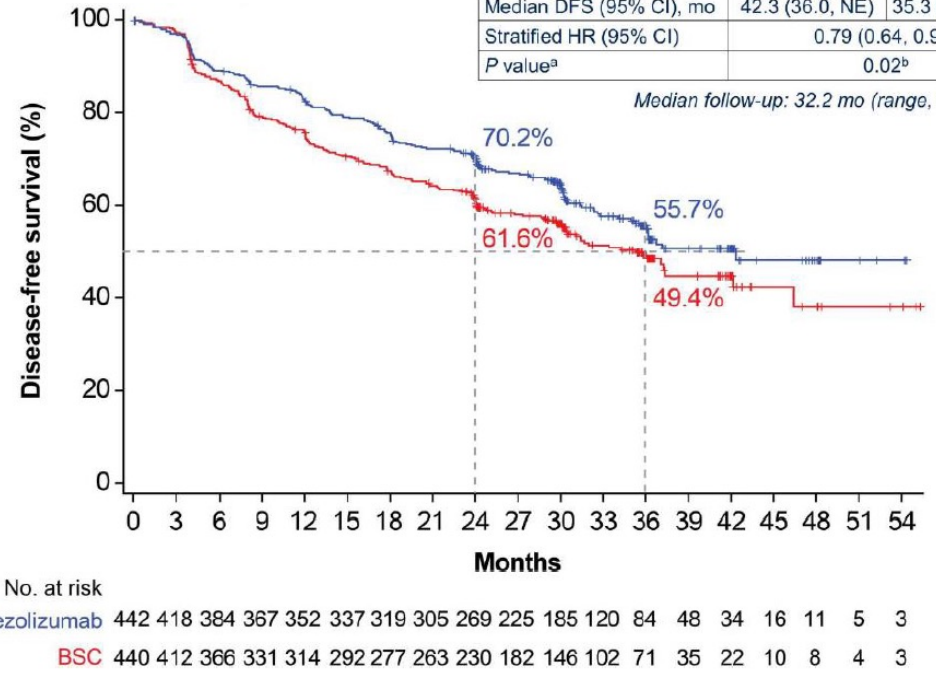
IMpower010: Summary of results

What we already knew

	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[a]	0.02[b]	



Wakelee ASCO 2021, Altorki WCLC 2021

DFS benefit in stage II-IIIA (UICC/AJCC v7)

Absence of benefit

- . PD-L1 <1% (45.4%)
- . Pneumonectomy (15.9%)
- . EGFRmut/ALK+ (11.6%/3.3%)

Stage IB (12.2%) ?

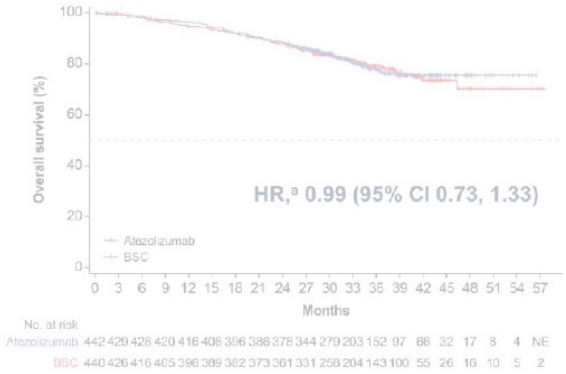
Benjamin Besse. ESMO 2021; Discussant.

RTP RESEARCH TO PRACTICE

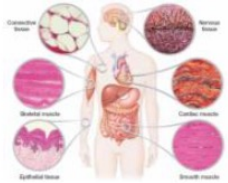
The Yin and the Yang of the immune system

Hyperprogression of the micrometastic disease

Overall Survival, stage II-IIIA



Delayed side effects



Immediate side effects reported

imAEs in ≥1% of patients

	Atezolizumab (n=495)		BSC (n=495)	
n (%)	Any grade	Grade 3-4	Any grade	Grade 3-4
Any immune-mediated AEs	256 (51.7)[b]	39 (7.9%)	47 (9.5)	5 (0.6)

51.7% any grade, 7.9% grade 3-4
12.1% requiring steroids
1 grade 5

› JAMA Oncol. 2021 May 1;7(5):744-748. doi: 10.1001/jamaoncol.2021.0051.

Chronic Immune-Related Adverse Events Following Adjuvant Anti-PD-1 Therapy for High-risk Resected Melanoma

43.2% developed chronic irAEs (>12 wks after discontinuation)

96% grade 1-2

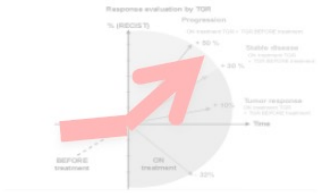
endocrinopathies (83.0%), arthritis (48.9%), xerostomia (52.9%), neurotoxicities (73.3%), and ocular events (62.5%)

Benjamin Besse. ESMO 2021; Discussant.

RTP RESEARCH TO PRACTICE

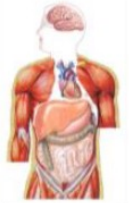
The Yin and the Yang of the immune system

Hyperprogression of the micrometastic disease

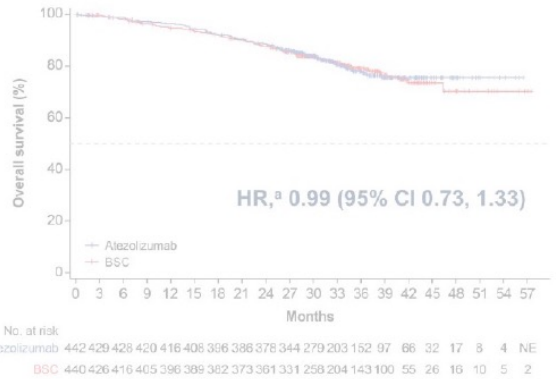


Delayed side effects

Second Cancer



Overall Survival, stage II-IIIA



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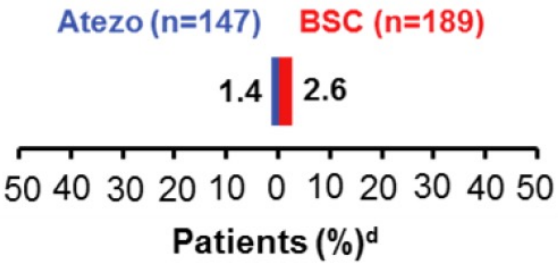
n (%)	Any grade	Grade 3-4	Any grade	Grade 3-4
Any immune-mediated AEs	256 (51.7)[b]	39 (7.9%)	47 (9.5)	5 (0.6)

51.7% any grade, 7.9% grade 3-4
12.1% requiring steroids
1 grade 5

2nd primary lung, stage II-IIIA



Benjamin Besse. ESMO 2021; Discussant.

The 2020 decade fight

Neoadjuvant

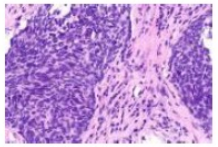
Better to treat with primary tumor?

Rate of drop off?

Surgery procedure : more difficult?

Maybe 4 cycles of IO is enough

pCR/MPR surrogate of OS?



Adjuvant

Better if tumor burden is lower?

Less eligible patients?

Surgery vs. immune system?

1 yr IO too much or not enough?

More easy to assess biomakers

Benjamin Besse. ESMO 2021; Discussant.

Journal Club with Dr Naidoo (Part 1)

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What about the microbiome!

What relative and absolute risk numbers should be offered to interested patients after these benefits and risks?

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2021 ASCO ANNUAL MEETING

THE MICROBIOME, RACIAL DISPARITIES AND NEOADJUVANT STRATEGIES

Jarushka Naidoo, MB BCH MHS

Beaumont Hospital/RCSI University Dublin, Ireland

Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University

May 21, 2021

Pan-Cancer Intratumor Microbiome
Summary

Strengths:

- Large number of potential microbial RNA species identified from TCGA, as per prior studies
- First analysis examining associations between intratumoral microbiome and clinical features
- Race is likely to affect the host microbiota, reasonable microbiota by tumor type and race
- Results reflected known differences in cancer outcome by race (breast cancer in AA patients)

Challenges:

- TCGA samples not collected in a manner that controlled for microbial contamination (multiple filters)
- FDR correction for multiple hypothesis testing
- Several factors may impact intratumoral microbiota and clinical outcomes
  - gender, age , diet, medications, prior cancer therapy
  - multivariate analysis would be useful incorporating confounders and interaction terms

Presented By: Jarushka Naidoo, MB BCH MHS
Beaumont Hospital/RCSI, Johns Hopkins University

2021 ASCO ANNUAL MEETING

Naidoo J. ASCO 2021 Discussant: Microbiome racial disparities and neoadjuvant strategies.

Cancer Treatment Reviews 104 (2022) 102350

Contents lists available at ScienceDirect

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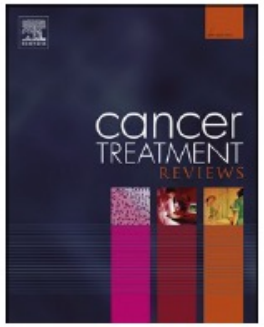
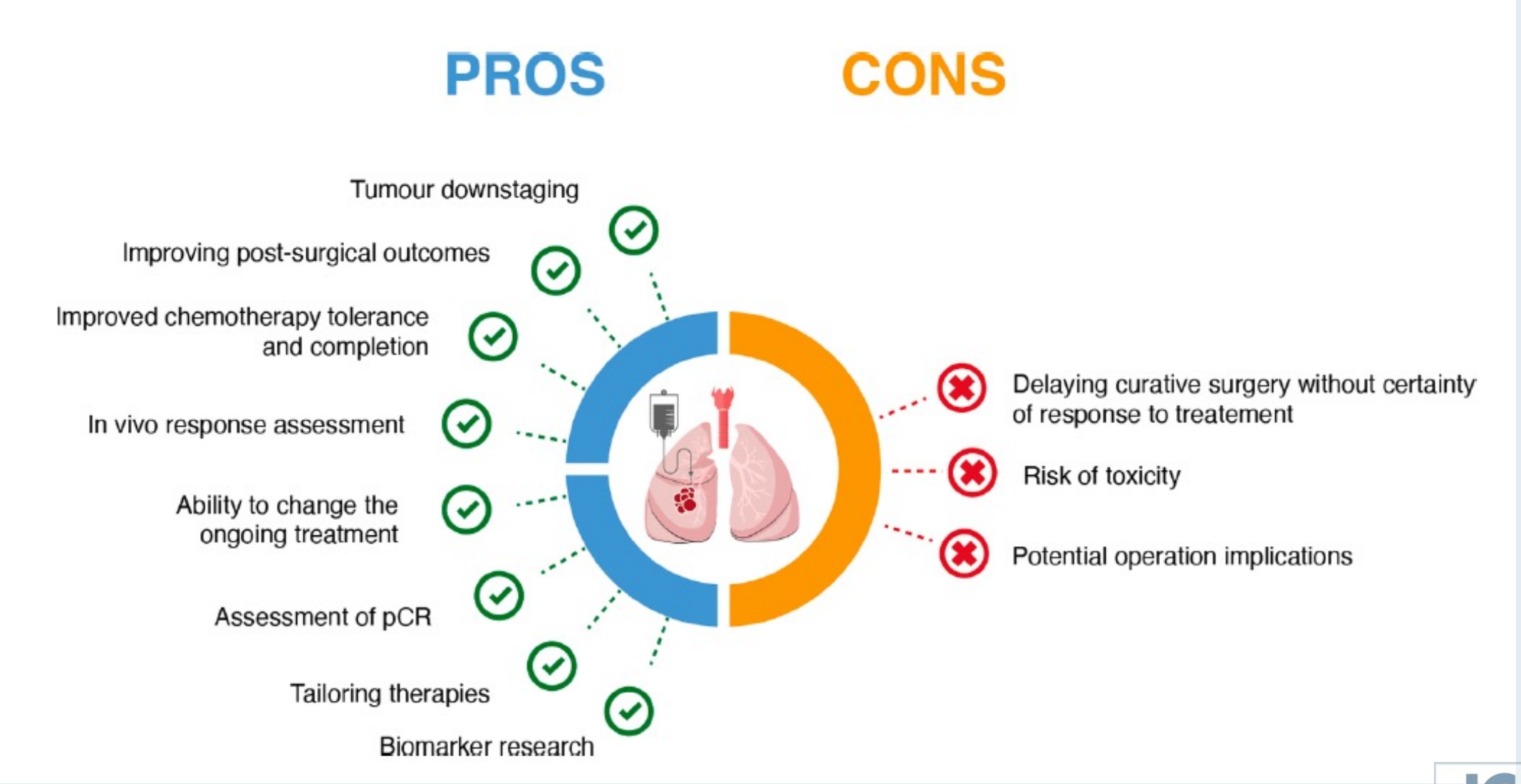
journal homepage: www.elsevier.com/locate/ctrv



Role and impact of immune checkpoint inhibitors in neoadjuvant treatment for NSCLC

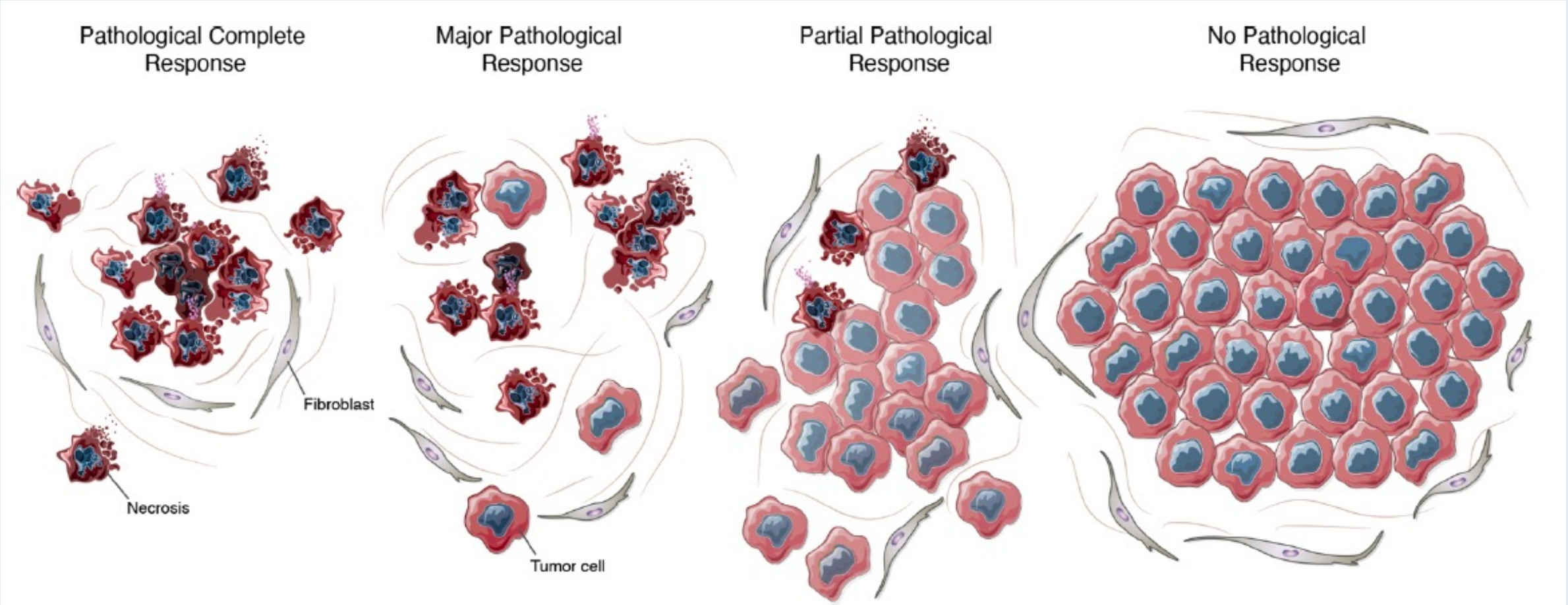
Alex Friedlaender [a,g], Jarushka Naidoo [b,c], Giuseppe Luigi Banna [d], Giulio Metro [e], Patrick Forde [f], Alfredo Addeo [a,*]

Potential Pros and Cons of Neoadjuvant Therapy in NSCLC



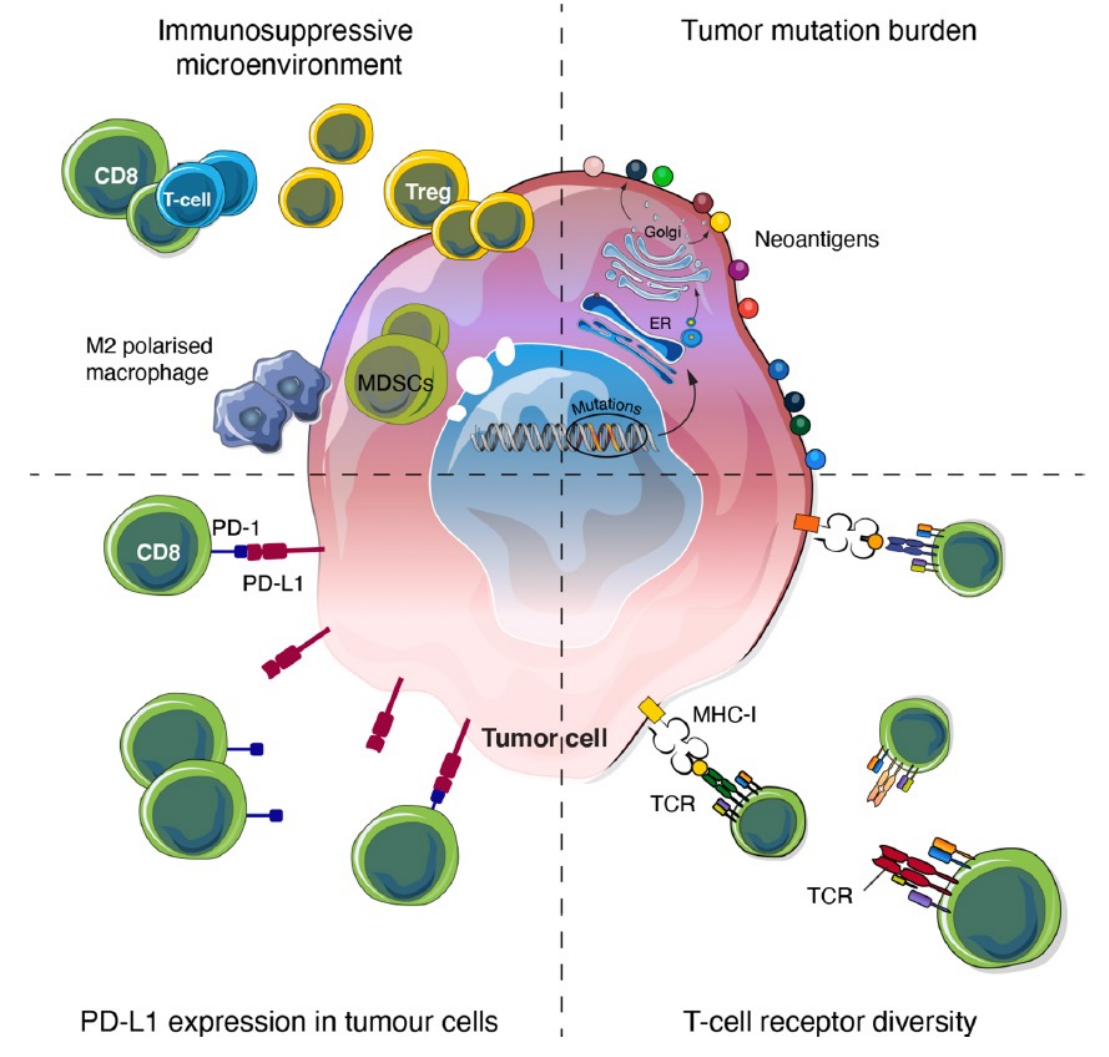
Friedlaender A et al. *Cancer Treat Rev* 2022;[Online ahead of print].

Depth of Pathologic Response to Neoadjuvant Therapy



Friedlaender A et al. *Cancer Treat Rev* 2022;[Online ahead of print].

Potential Predictive Biomarkers of Response to Neoadjuvant Immunotherapy



Friedlaender A et al. *Cancer Treat Rev* 2022;[Online ahead of print].

Meet The Professor with Dr Naidoo

Introduction

MODULE 1: Adjuvant and Neoadjuvant Immunotherapy

MODULE 2: Consolidation Immunotherapy After Chemoradiation for Unresectable Locally Advanced Non-Small Cell Lung Cancer

- Dr Jasani: A 45-year-old woman with localized NSCLC and an EGFR exon 19 mutation – PD-L1 <1%

MODULE 3: Immunotherapy for Metastatic Disease

MODULE 4: Special Considerations in Immunotherapy: Acute and Delayed Toxicity; Cure?

MODULE 5: Immunotherapy in Mesothelioma

MODULE 6: Immunotherapy and Novel Agents in Small Cell Lung Cancer

Case Presentation: A 45-year-old woman with Stage IIIA NSCLC and an EGFR exon 19 mutation – PD-L1 <1%

Dr Nikesh Jasani (Houston, Texas)

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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?

 Dr Aggarwal	Observation	 Dr Hanna	No further therapy
 Dr Goldberg	Durvalumab	 Dr Liu	Osimertinib
 Dr Govindan	Durvalumab	 Dr Ramalingam	Durvalumab

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Journal Club with Dr Naidoo (Part 2)

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TO PRACTICE

Lung Cancer: Targets and Therapy

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REVIEW

Immunotherapy for Stage III NSCLC: Durvalumab and Beyond

Orla Fitzpatrick[1]
Jarushka Naidoo[1,2]

Lung Cancer (Auckl) 2021;12:123-31.

original reports

Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

David R. Spigel, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Jhanelle E. Gray, MD[3]; David Vicente, MD[4]; David Planchard, MD, PhD[5]; Luis Paz-Ares, MD, PhD[6]; Johan F. Vansteenkiste, MD, PhD[7]; Marina C. Garassino, MD[8,9]; Rina Hui, PhD[10]; Xavier Quantin, MD, PhD[11]; Andreas Rimner, MD[12]; Yi-Long Wu, MD[13]; Mustafa Özgüroğlu, MD[14]; Ki H. Lee, MD[15]; Terufumi Kato, MD[16]; Maike de Wit, MD, PhD[17]; Takayasu Kurata, MD[18]; Martin Reck, MD, PhD[19]; Byoung C. Cho, MD, PhD[20]; Suresh Senan, PhD[21]; Jarushka Naidoo, MBBCH, MHS[22]; Helen Mann, MSc[23]; Michael Newton, PharmD[24]; Piruntha Thiyagarajah, MD[23]; and Scott J. Antonia, MD, PhD[3]; on behalf of the PACIFIC Investigators

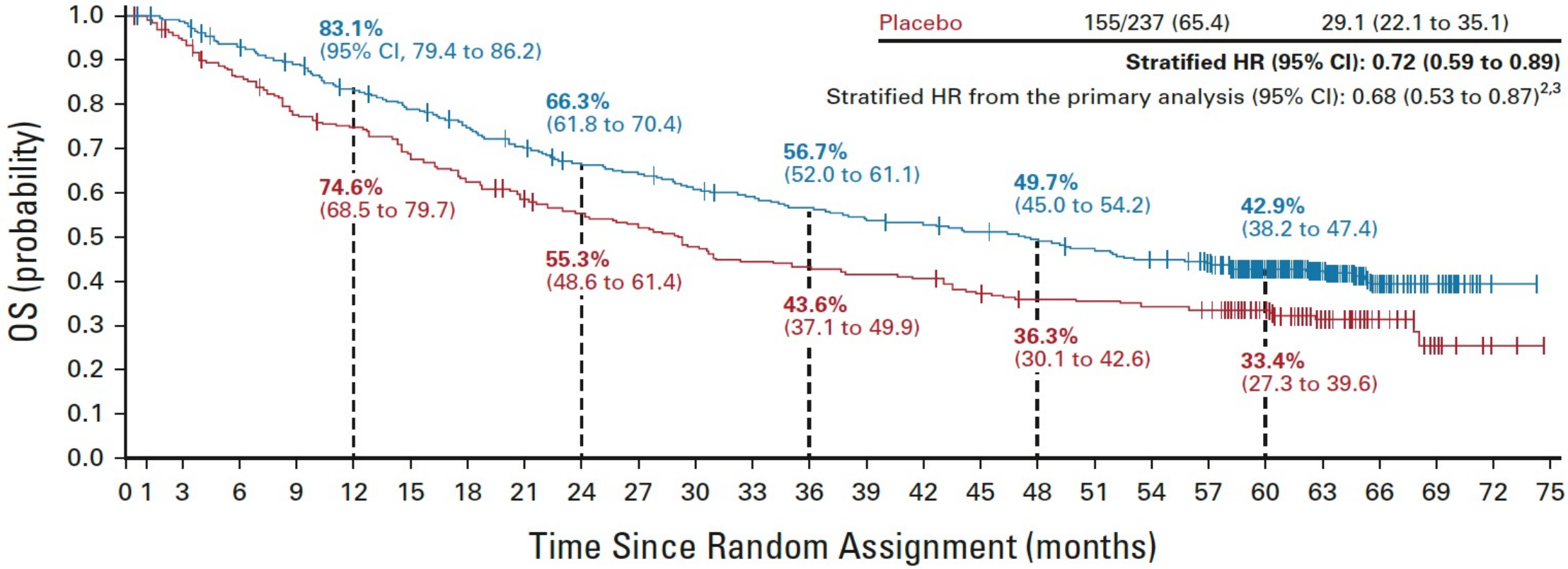
J Clin Oncol 2022;[Online ahead of print].

PACIFIC: Five-Year Overall Survival (OS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC

Arm	No. of Events/ Total No. of Patients (%)	Median OS (95% CI), Months
Durvalumab	264/476 (55.5)	47.5 (38.1 to 52.9)
Placebo	155/237 (65.4)	29.1 (22.1 to 35.1)

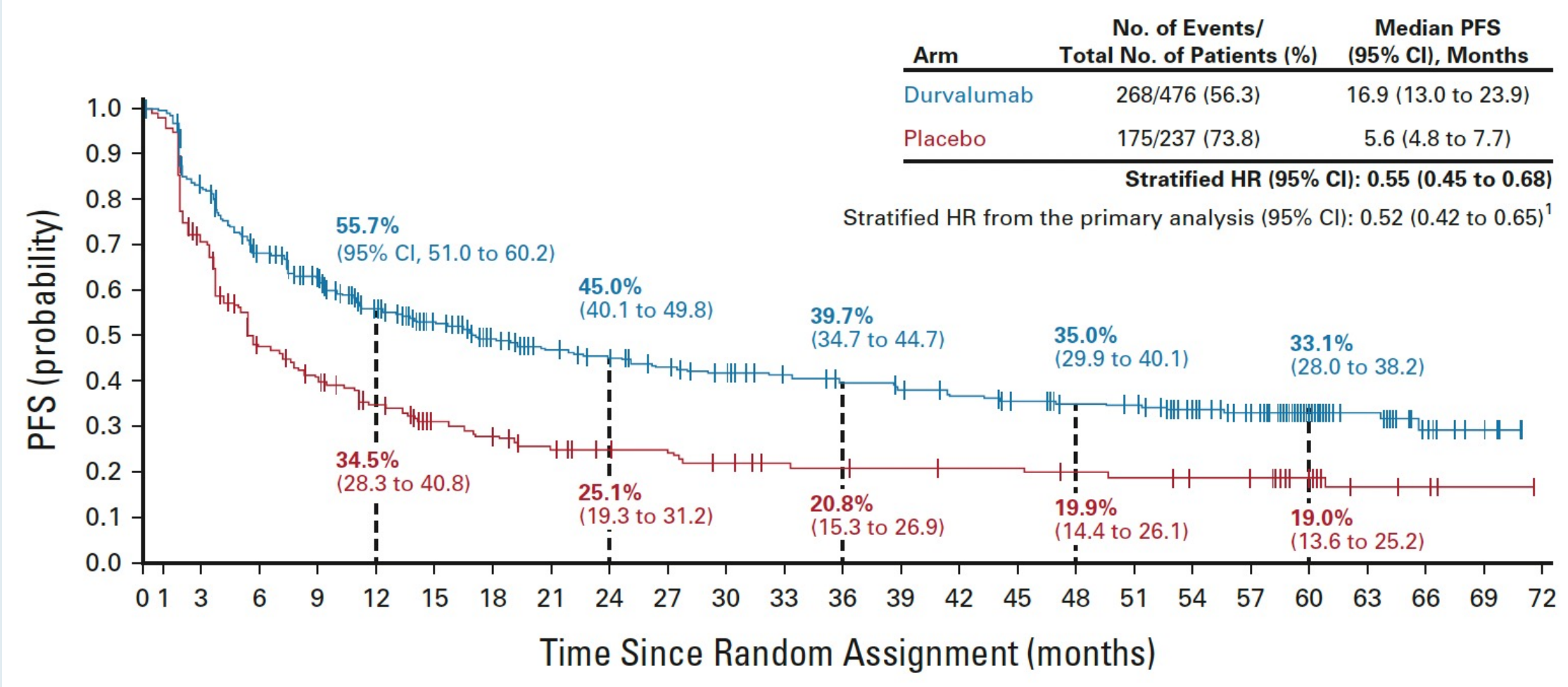
Stratified HR (95% CI): 0.72 (0.59 to 0.89)

Stratified HR from the primary analysis (95% CI): 0.68 (0.53 to 0.87)[2,3]



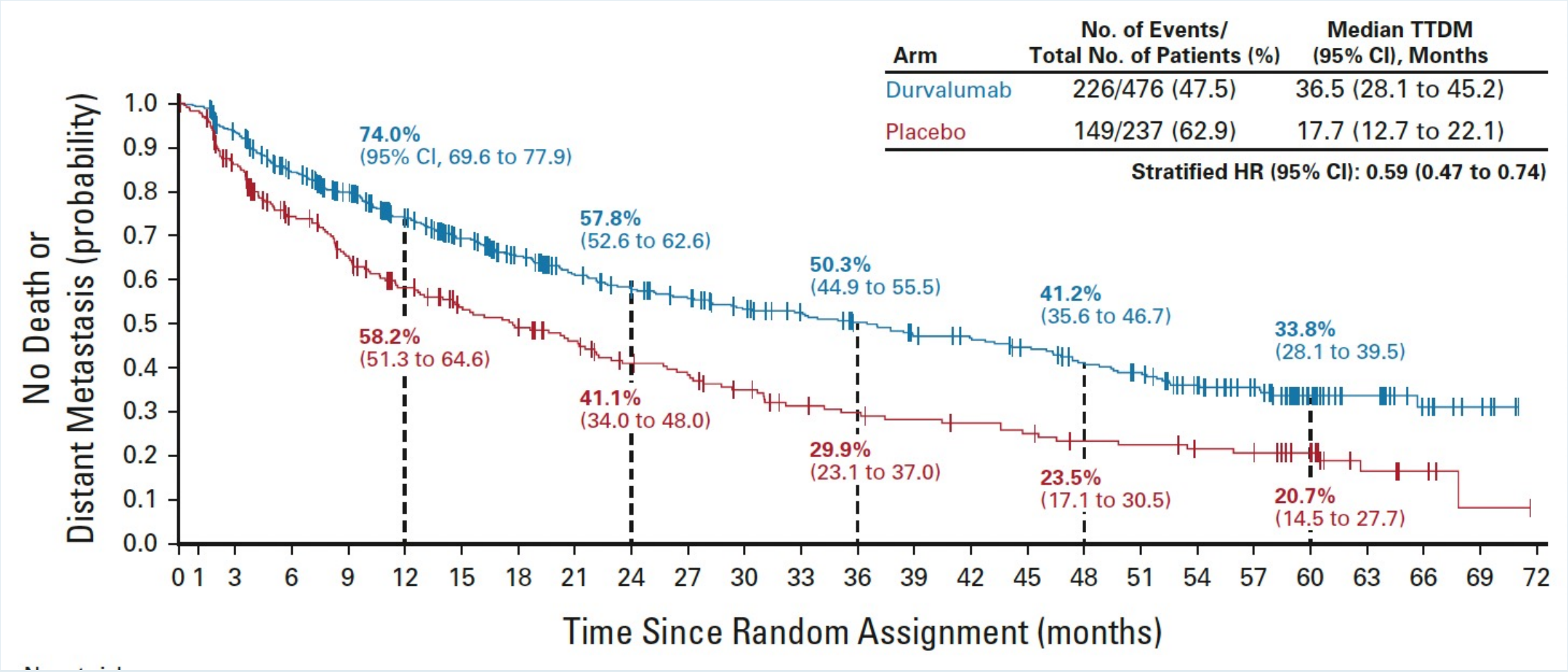
Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

PACIFIC: Five-Year Progression-Free Survival (PFS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

PACIFIC: Updated Time to Death or Distant Metastasis (TTDM) — BICR in the ITT Population



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

Meet The Professor with Dr Naidoo

Introduction

MODULE 1: Adjuvant and Neoadjuvant Immunotherapy

MODULE 2: Consolidation Immunotherapy After Chemoradiation for Unresectable Locally Advanced Non-Small Cell Lung Cancer

MODULE 3: Immunotherapy for Metastatic Disease

- Dr Kumar: A 75-year-old man with metastatic adenocarcinoma of the lung and MET amplification with PD-L1 90%
- Dr Gupta: A 58-year-old woman with microsatellite-stable adenocarcinoma of the lung with an NRG1 fusion mutation and CNS metastases
- Dr Lobins: A 63-year-old man with metastatic adenocarcinoma of the lung who receives carboplatin, pemetrexed and pembrolizumab

MODULE 4: Special Considerations in Immunotherapy: Acute and Delayed Toxicity; Cure?

MODULE 5: Immunotherapy in Mesothelioma

MODULE 6: Immunotherapy and Novel Agents in Small Cell Lung Cancer

RTP RESEARCH TO PRACTICE

Case Presentation: A 75-year-old man with metastatic adenocarcinoma of the lung and MET amplification with PD-L1 90%

Dr KS Kumar (New Port Richey, Florida)

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Case Presentation: A 58-year-old woman with MSS adenocarcinoma of the lung with an NRG1 fusion mutation and CNS metastases

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 63-year-old man with metastatic adenocarcinoma of the lung who receives carboplatin, pemetrexed and pembrolizumab

Dr Raymond Lobins (Mentor, Ohio)

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Which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 0%?

 Dr Aggarwal	Carboplatin/pemetrexed/ pembrolizumab	 Dr Hanna	Carboplatin/pemetrexed/ pembrolizumab
 Dr Goldberg	Carboplatin/pemetrexed/ pembrolizumab	 Dr Liu	Carboplatin/pemetrexed/ pembrolizumab
 Dr Govindan	Carboplatin/pemetrexed/ pembrolizumab	 Dr Ramalingam	Ipilimumab/nivolumab

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FDA-Approved Single-Agent Immunotherapy Options for First-Line Therapy

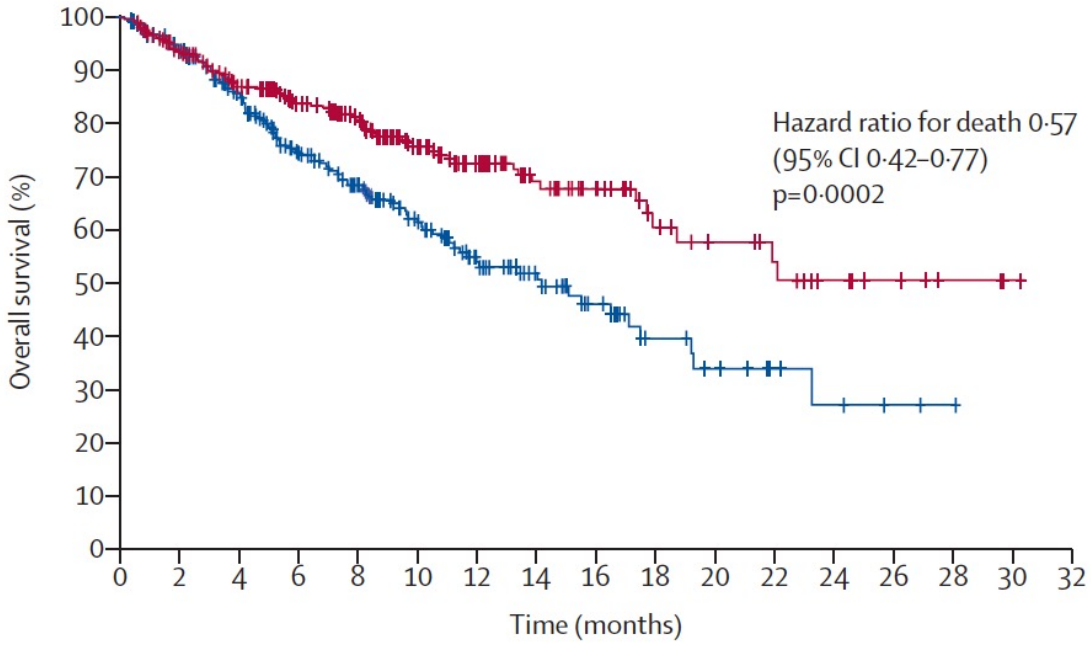
Monotherapy	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab[1,2] (q3wk or q6wk)	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS ≥1%	0.63
Atezolizumab[3] (q2wk, q3wk or q4wk)	5/18/20	IMpower110	PD-L1 TPS ≥50, EGFR and/or ALK wt	0.59
Cemiplimab[4] (q3wk)	2/22/21	EMPOWER-Lung 1 (Study 1624)	PD-L1 TPS ≥50, EGFR and/or ALK and/or ROS1 wt	0.57

[1] Mok. *Lancet* 2019. [2] Reck. *J Clin Oncol* 2019. [3] Herbst. *N Engl J Med* 2020. [4] Sezer. *Lancet* 2021.

EMPOWER-Lung 1: A Phase III Trial of Cemiplimab Monotherapy for First-Line Treatment of NSCLC with PD-L1 ≥50%

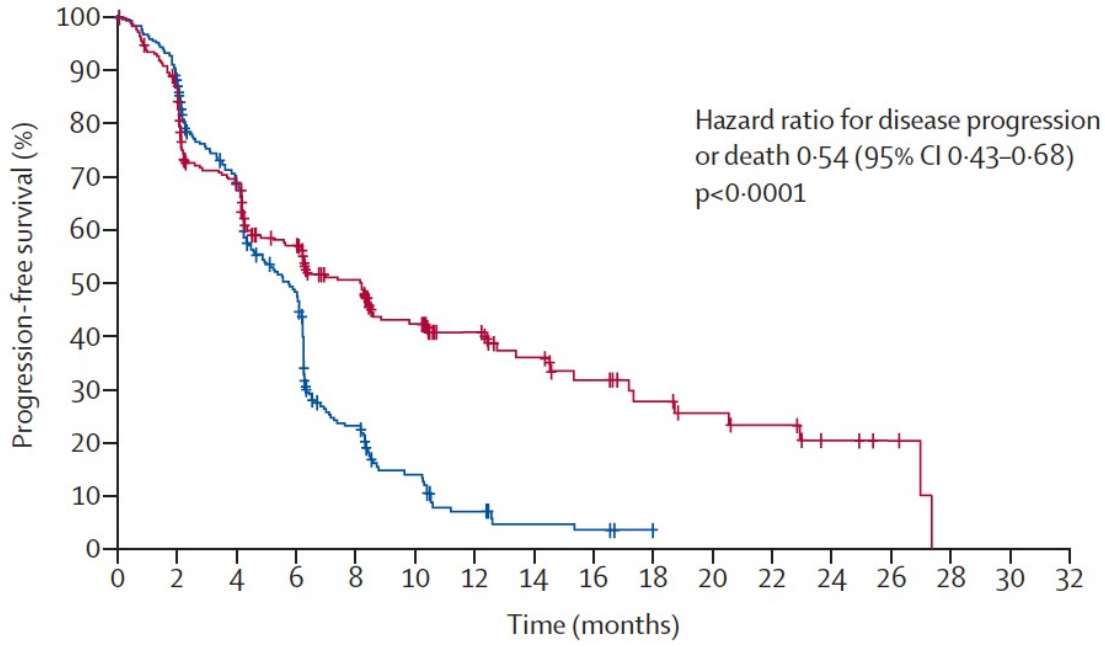
Overall Survival

	Number of patients	Median overall survival months (95% CI)
Cemiplimab	283	Not reached (95% CI 17·9–NE)
Chemotherapy	280	14·2 (95% CI 11·2–17·5)



Progression-Free Survival

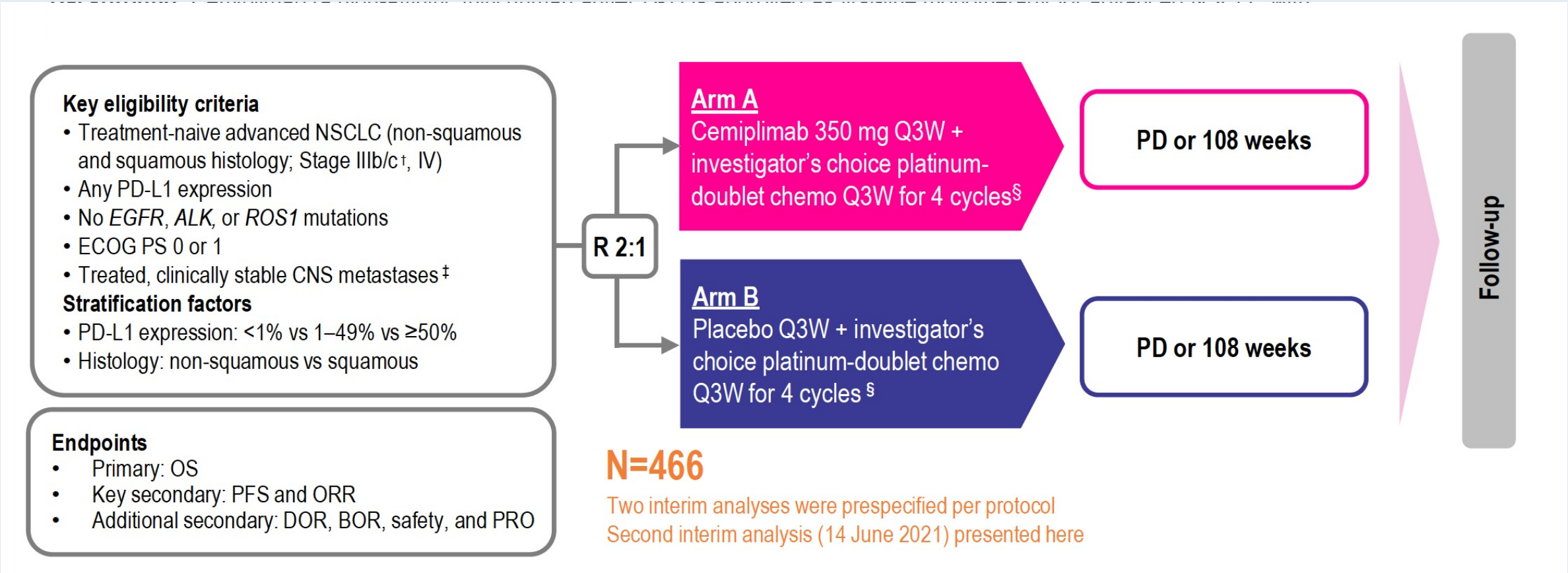
	Number of patients	Median progression-free survival months (95% CI)
Cemiplimab	283	8·2 (95% CI 6·1–8·8)
Chemotherapy	280	5·7 (95% CI 4·5–6·2)



Sezer A et al. *Lancet* 2021;397:592-604.

RTP RESEARCH TO PRACTICE

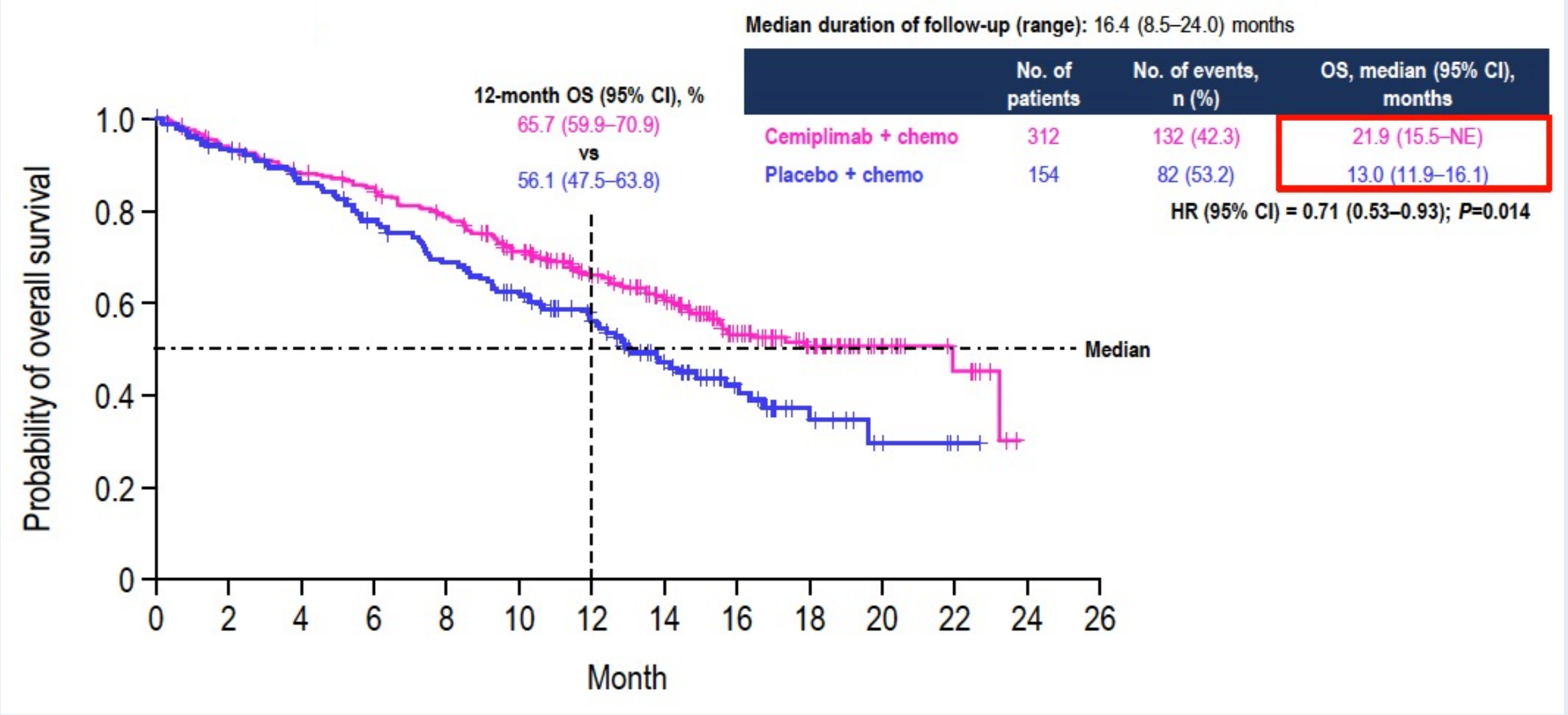
EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC



Gogishvili M et al. ESMO 2021;Abstract LBA51.

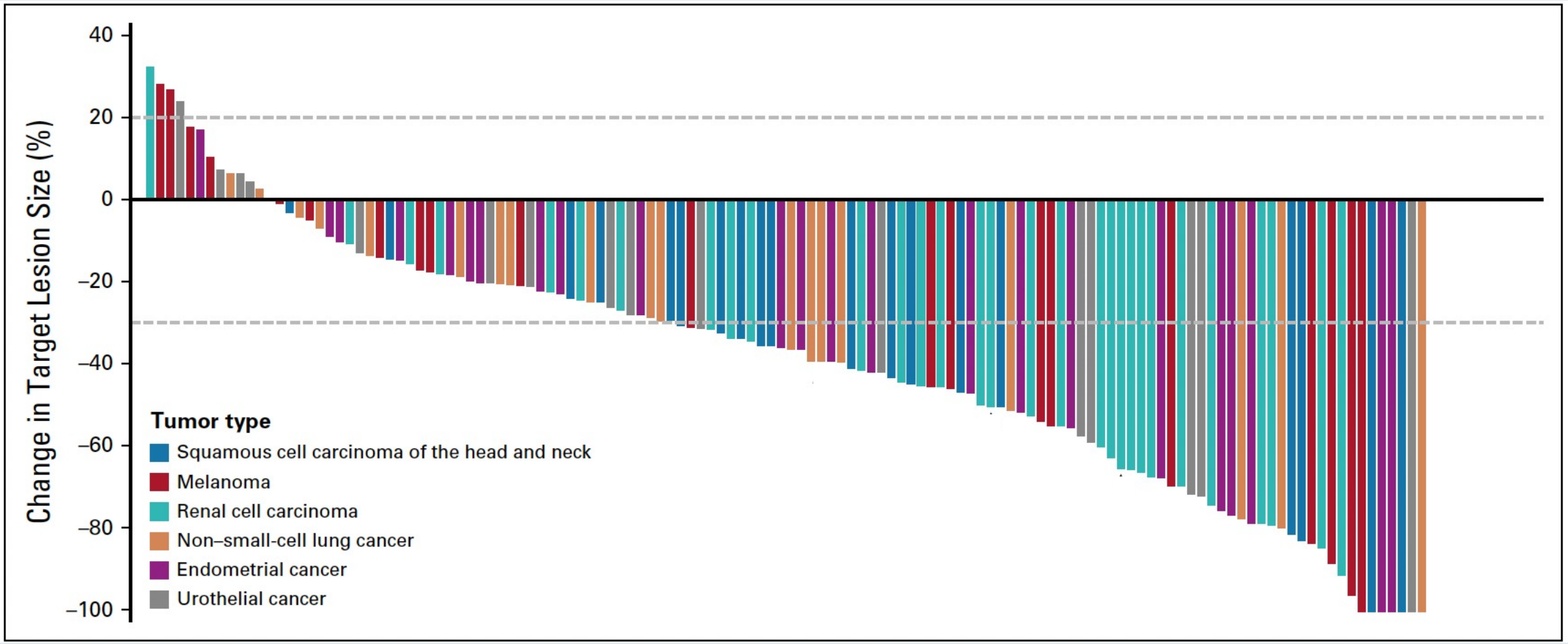
RTP RESEARCH TO PRACTICE

EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC



Gogishvili M et al. ESMO 2021;Abstract LBA51.

KEYNOTE-146: Maximum Change in Target Lesion Size (All Patients)



Taylor MH et al. *J Clin Oncol* 2020;38:154-63.

KEYNOTE-146: Phase IB/II Trial of Lenvatinib/Pembrolizumab in Advanced Solid Cancers

Efficacy in the Metastatic NSCLC Population				
N	**Line of therapy**	**ORR**	**Median DOR**	**Median PFS**
21	Any	33%	10.9 mo	5.9 mo

DOR = duration of response

Summary of Treatment-Related Adverse Events (TREAs): All Patients	
Parameter	**(N = 137)**
Serious AEs	26%
TREAs leading to pembrolizumab dose interruption	45%
TREAs leading to pembrolizumab discontinuation	15%
TREAs leading to lenvatinib dose reduction and/or interruption	85%
TREAs leading to lenvatinib discontinuation	13%

Taylor MH et al. *J Clin Oncol* 2020;38:154-63.

Ongoing LEAP Phase III Trials in NSCLC

Trial ID	N	Patient population	Line of therapy	Treatment
LEAP-006	726	Previously untreated metastatic nonsquamous NSCLC	1L	• Pemetrexed + platinum chemo + Pembrolizumab + lenvatinib • Pemetrexed + platinum chemo + pembrolizumab + placebo
LEAP-007	620	Previously untreated, advanced (Stage IV), PD-L1 positive (TPS ≥1%) NSCLC	1L	• Lenvatinib + pembrolizumab • Placebo + pembrolizumab
LEAP-008	405	Metastatic NSCLC that progressed during/after platinum doublet chemotherapy or on treatment with anti-PD-1/PD-L1 monoclonal antibody as monotherapy or combination therapy	≥2L	• Lenvatinib + pembrolizumab • Standard chemotherapy • Lenvatinib

Taylor MH et al. *Futur Oncol* 2021;17(6):637-47. www.clinicaltrials.gov. NCT03829319, NCT03829332, NCT03976375. Accessed November 2021.

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Background: Tiragolumab, an Anti-TIGIT Antibody

- Tiragolumab is a fully human IgG1/kappa anti-TIGIT monoclonal antibody with an intact Fc region that blocks the binding of TIGIT to its receptor PVR

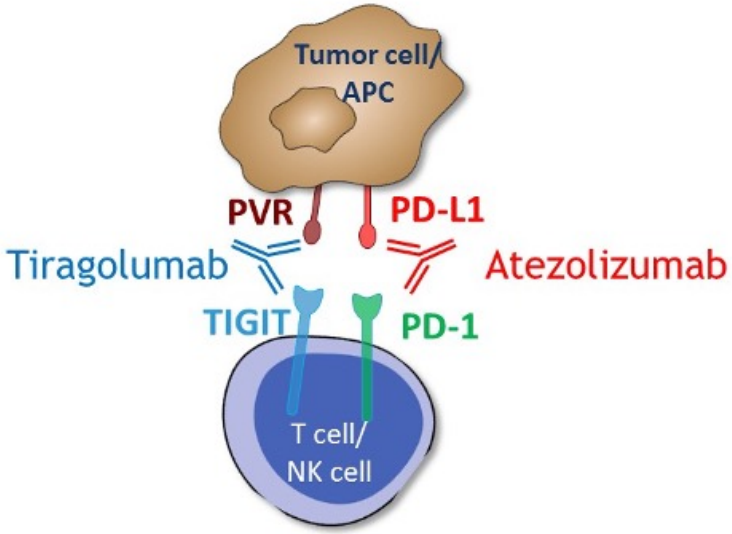
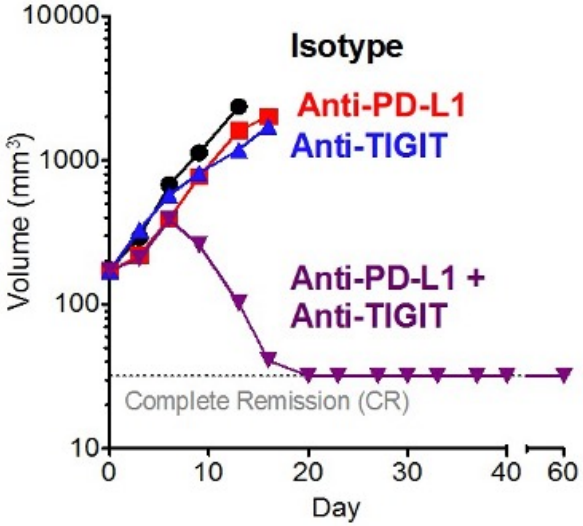


Figure adapted from Manieri et al. *Trends Immunology* 2017

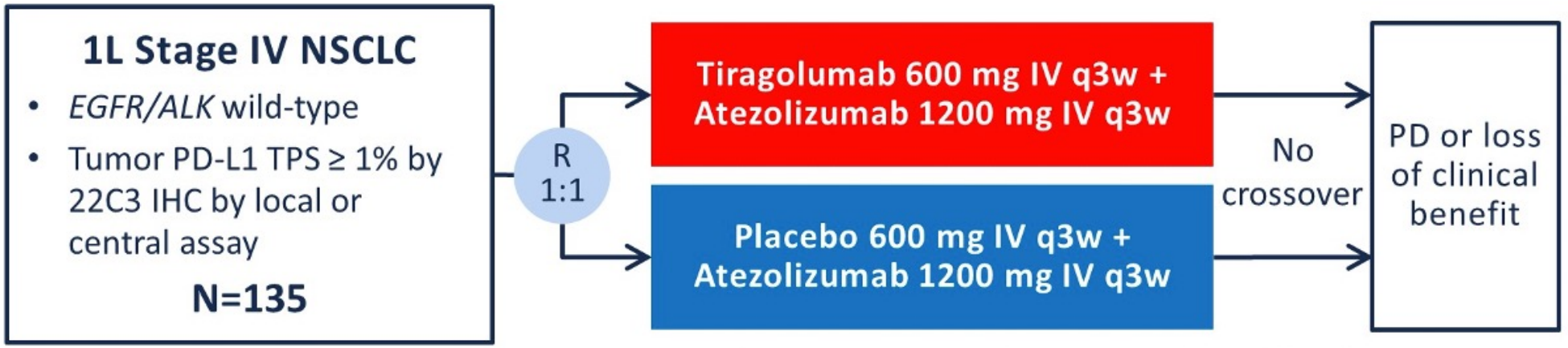
- In preclinical models, combination treatment with anti-TIGIT and anti-PD-L1 antibodies synergistically improves tumor control and prolongs survival in mice[1]



[1] Johnston et al. *Cancer Cell* 2014

Rodriguez-Abreu D et al. ASCO 2020;Abstract 9503.

CITYSCAPE Study Design



Stratification Factors:

- PD-L1 TPS (1-49% vs ≥ 50%)
- Histology (Non-Squamous vs Squamous)
- Tobacco use (yes vs no)

- **Co-Primary Endpoints: ORR** and **PFS**
- **Key Secondary Endpoints: Safety**, DOR, OS, Patient-reported outcomes (PROs)
- **Exploratory Endpoints:** Efficacy analysis by PD-L1 status

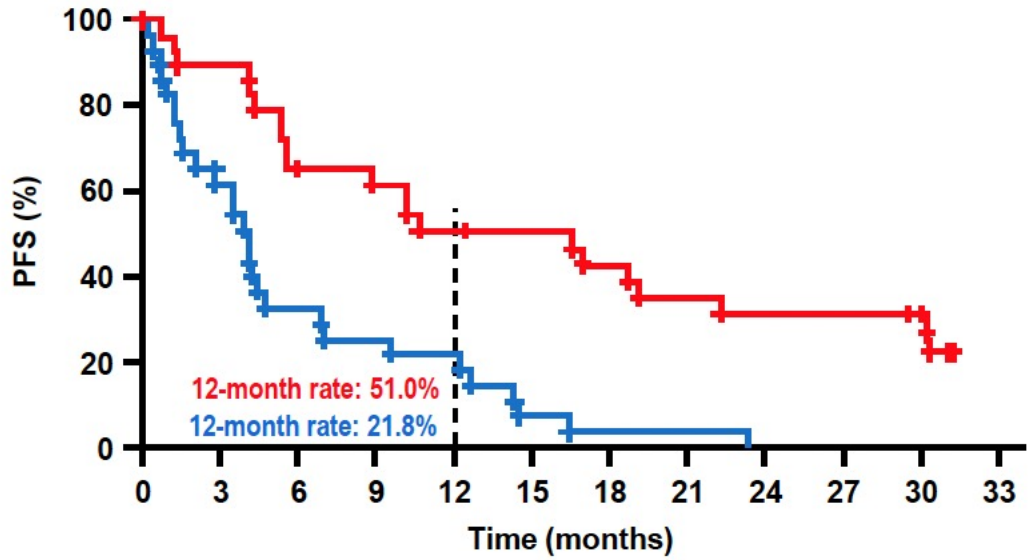
DOR = duration of response; IHC = immunohistochemistry; ORR = confirmed overall response rate; OS = overall survival; PD = progressive disease; PFS = progression free survival ; q3w = every 3 weeks; R = randomized; TPS = tumor proportion score

Rodriguez-Abreu D et al. ASCO 2020;Abstract 9503.

CITYSCAPE: PFS by PD-L1 Subgroup

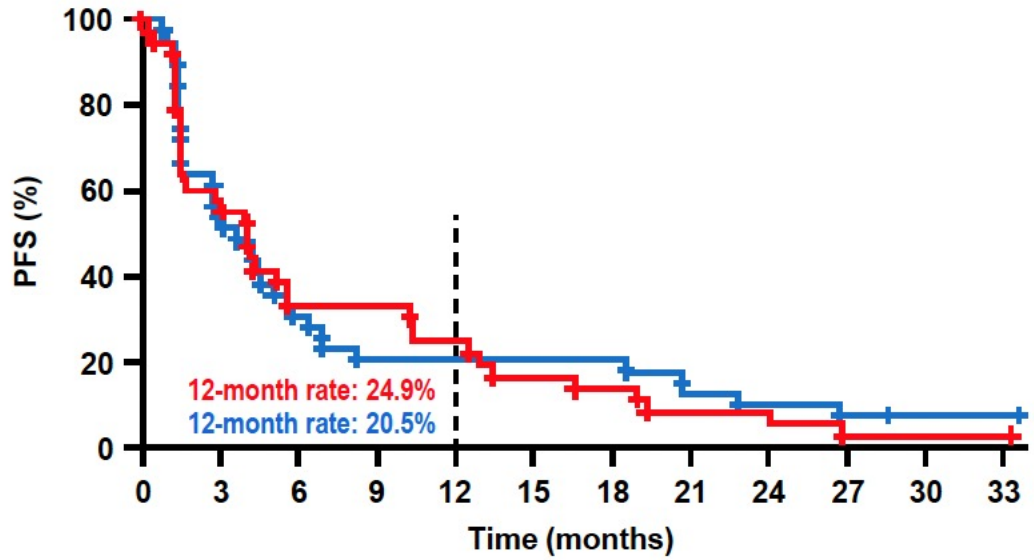
PD-L1 TPS ≥50% (n=58)

	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	21 (72.4)	16.6 (5.5–22.3)	0.29* (0.15–0.53)	69.0	15.7 (9.1–NE)
Placebo + atezo	28 (96.6)	4.1 (2.1–6.8)		24.1	8.2 (5.6–10.4)



PD-L1 TPS 1–49% (n=77)

	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	36 (94.7)	4.0 (1.6–5.6)	1.07* (0.67–1.71)	15.8	17.8 (8.3–24.2)
Placebo + atezo	36 (92.3)	3.6 (1.4–5.5)		17.9	18.8 (15.9–22.8)



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

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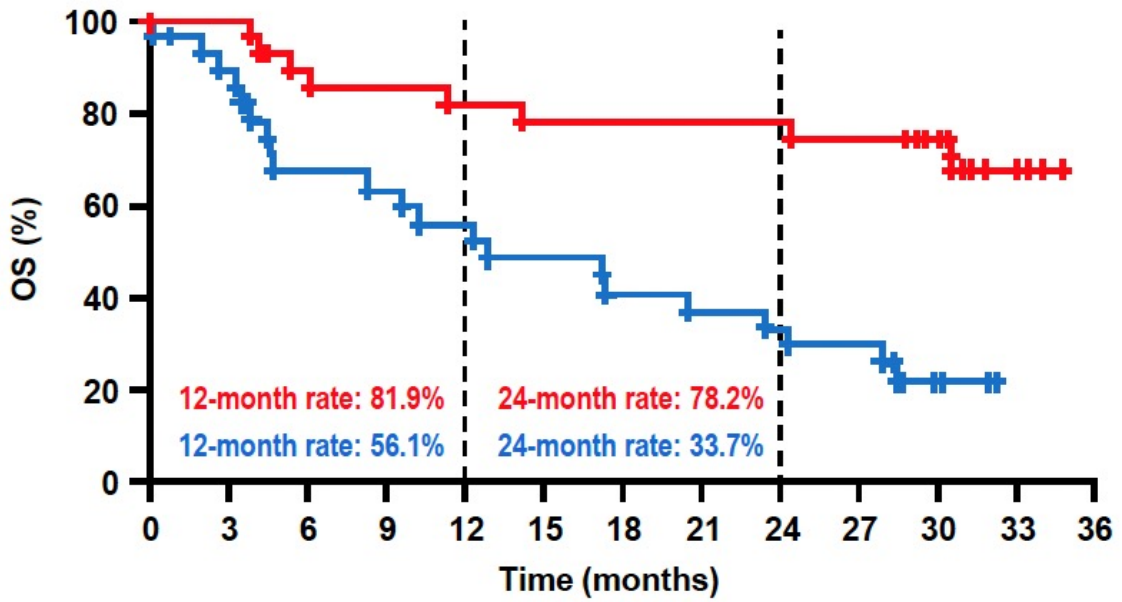
CITYSCAPE: OS by PD-L1 Subgroup

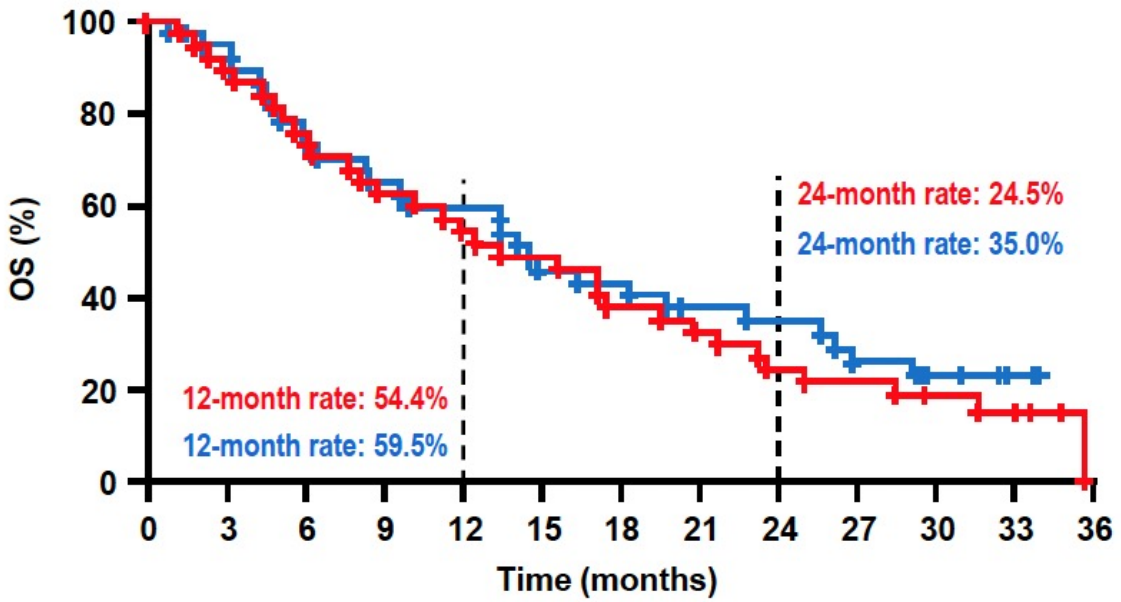
PD-L1 TPS ≥50% (n=58)

	Events n (%)	Median OS, months (95% CI)	HR (95% CI)
Tira + atezo	8 (27.6)	NE (30.3–NE)	0.23* (0.10–0.53)
Placebo + atezo	21 (72.4)	12.8 (4.7–24.2)	



PD-L1 TPS 1–49% (n=77)

	Events n (%)	Median OS, months (95% CI)	HR (95% CI)
Tira + atezo	32 (84.2)	13.3 (8.0–20.7)	1.16* (0.70–1.94)
Placebo + atezo	28 (71.8)	14.5 (8.3–25.6)	



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

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SKYSCRAPER-02: A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of Atezolizumab plus Carboplatin and Etoposide with or without Tiragolumab in Patients with Untreated Extensive-Stage SCLC

Meet The Professor with Dr Naidoo

Introduction

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- Dr Gosain: A 74-year-old woman with unresectable squamous cell lung cancer (PD-L1 25%) develops pruritus during durvalumab consolidation therapy
- Dr Gupta: A 52-year-old woman with MSS adenocarcinoma of the lung and brain metastases

MODULE 5: Immunotherapy in Mesothelioma

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Case Presentation: A 74-year-old woman with unresectable squamous cell lung cancer (PD-L1 25%) develops pruritus during durvalumab consolidation therapy

Dr Rohit Gosain (Jamestown, New York)

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Case Presentation: A 52-year-old woman with MSS adenocarcinoma of the lung and brain metastases

Dr Ranju Gupta (Bethlehem, Pennsylvania)

Microsatellite status - MS-Stable

Tumor Mutational Burden - 4 Muts/Mb

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

ATM F2799fs*4

KRAS G10_A11insG

STK11 P281fs*6

IRF2 splice site 87+1G>A

NFKBIA amplification

NKX2-1 amplification

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Journal Club with Dr Naidoo (Part 3)

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ASCO special articles

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update

Bryan J. Schneider, MD[1]; Jarushka Naidoo, MD[2,3]; Bianca D. Santomasso, MD, PhD[4]; Christina Lacchetti, MHSc[5]; Sherry Adkins, MS[6]; Milan Anadkat, MD[7]; Michael B. Atkins, MD[8]; Kelly J. Brassil, PhD[6]; Jeffrey M. Caterino, MD, MPH[9]; Ian Chau, MD[10]; Marianne J. Davies, DNP[11]; Marc S. Ernstoff, MD[12]; Leslie Fecher, MD[1]; Monalisa Ghosh, MD[13]; Ishmael Jaiyesimi, DO, MS[14]; Jennifer S. Mammen, MD, PhD[15]; Aung Naing, MD[6], Loretta J. Nastoupil, MD[6]; Tanyanika Phillips, MD[16]; Laura D. Porter, MD[17]; Cristina A. Reichner, MD[18]; Carole Seigel, MBA[19], Jung-Min Song, MSN, RN, CNS[20]; Alexander Spira, MD, PhD[21]; Maria Suarez-Almazor, MD[6]; Umang Swami, MD[22]; John A. Thompson, MD[23]; Praveen Vikas, MD[24]; Yinghong Wang, MD[6]; Jeffrey S. Weber, MD, PhD[25]; Pauline Funchain, MD[20]; and Kathryn Bollin, MD[26]

J Clin Oncol 2021;39:4073-126.

Open access Original research

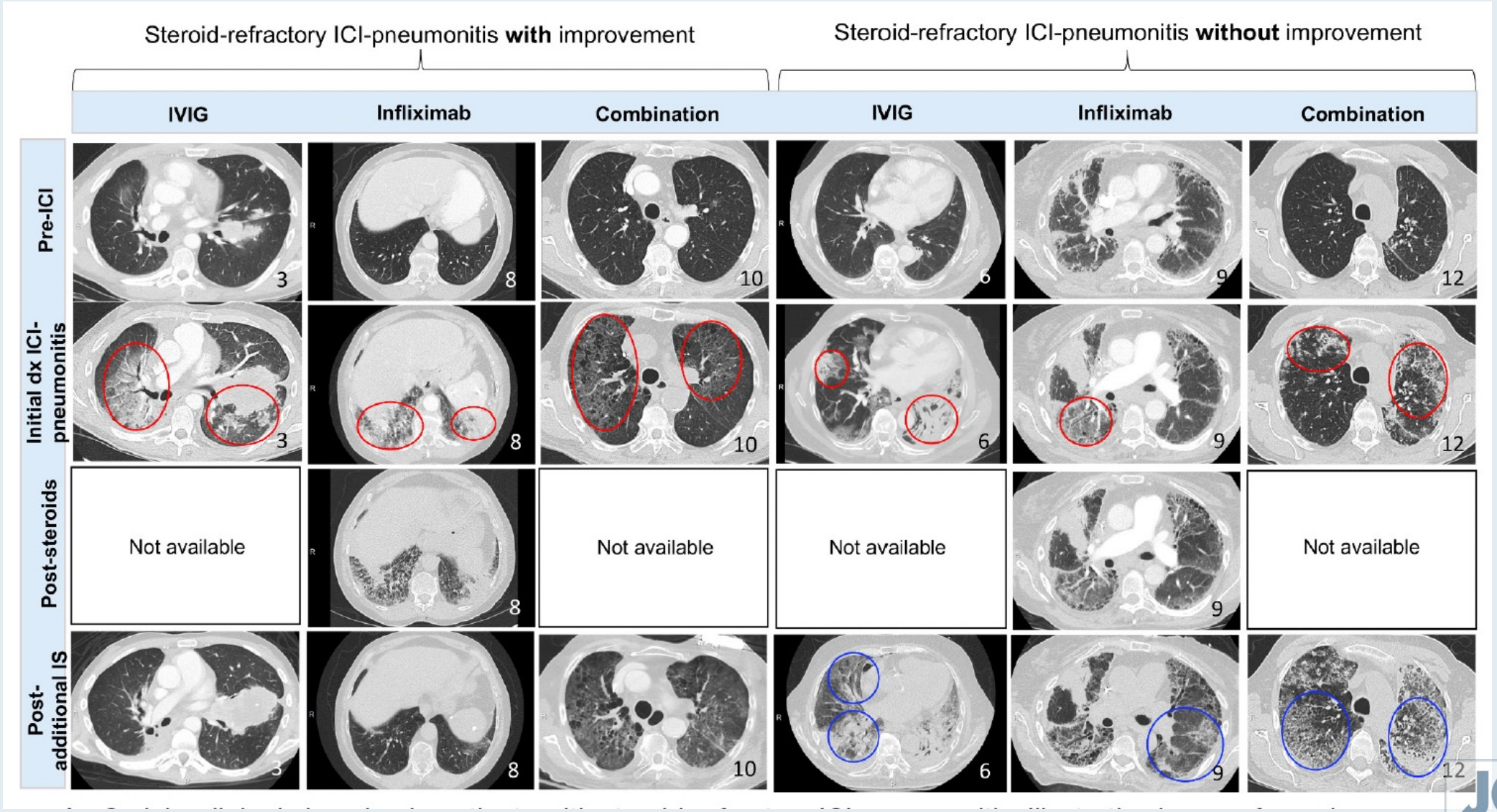
Journal for ImmunoTherapy of Cancer

Steroid-refractory PD-(L)1 pneumonitis: incidence, clinical features, treatment, and outcomes

Aanika Balaji ,[1,2] Melinda Hsu,[1,2] Cheng Ting Lin ,[3] Josephine Feliciano,[1,2] Kristen Marrone,[1,2] Julie R Brahmer,[1,2] Patrick M Forde,[1,2] Christine Hann,[1,2] Lei Zheng ,[1,2] Valerie Lee,[1,2] Peter B Illei,[1,4] Sonye K Danoff,[5] Karthik Suresh,[5] Jarushka Naidoo [1,2]

J Immunother Cancer 2021;9(1):e001731

Serial Radiologic Imaging in 6 Patients with Steroid-Refractory Immune Checkpoint Inhibitor (ICI) Pneumonitis with or without Improvement



Balaji A et al. *J Immunother Cancer* 2021;9(1):e001731.

Real-World Incidence and Management of Immune-Related Adverse Events from Immune Checkpoint Inhibitors: Retrospective Claims-Based Analysis

Victoria T. Brown, Dana Drzayich Antol, Patrick N. Racsa, Melea A. Ward & Jarushka Naidoo

Cancer Invest 2021;39(10):789-96.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Oncologist 2021;26(10):e1822-32

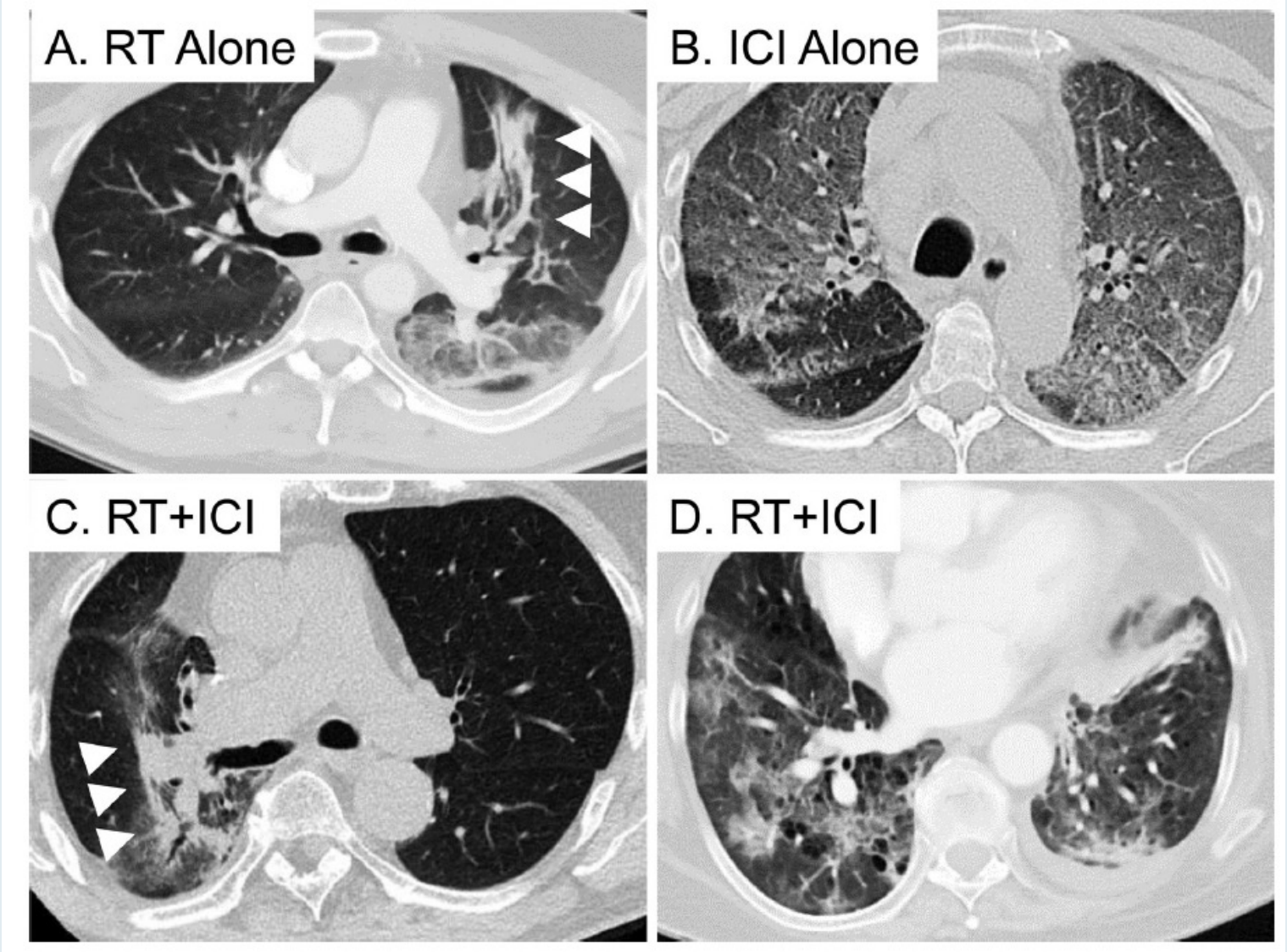
The Oncologist®

Lung Cancer

Radiation Versus Immune Checkpoint Inhibitor Associated Pneumonitis: Distinct Radiologic Morphologies

Xuguang Chen,[a] Khadija Sheikh,[a] Erica Nakajima,[d] Cheng Ting Lin,[b] Junghoon Lee,[a] Chen Hu,[c] Russell K. Hales,[a] Patrick M. Forde,[d] Jarushka Naidoo,[d] Khinh Ranh Voong[a]

Representative Computed Tomography Images of Radiation Therapy Pneumonitis



Chen X et al. *Oncologist* 2021;26(10):E1822-32.

nature COMMUNICATIONS

COMMENT

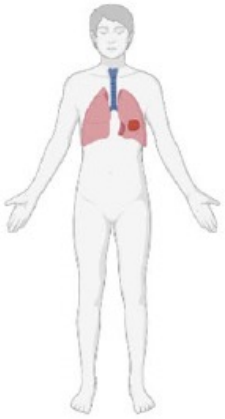
https://doi.org/10.1038/s41467-022-27960-2 OPEN

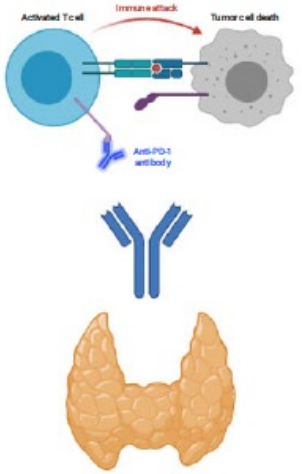
Immune-related adverse events and the balancing act of immunotherapy

Michael Conroy [1,2,3] & Jarushka Naidoo [1,2,3,4]✉

Nat Commun 2022;13(1):392

Innovation in Research of Immune-Related Adverse Events (irAEs)





Preclinical setting	irAE prevention	irAE diagnosis	irAE treatment
Improved preclinical irAE models	Genetic biomarkers of irAE risk	Biomarkers of irAEs	Prospective irAE clinical trials
Improved mechanisms of irAEs in preclinical models	Microbial biomarkers of irAE risk	Imaging of irAEs	
Identification of novel biomarkers of irAE	Interventions to mitigate irAE risk e.g. microbial manipulation	Improved diagnostic pathways e.g. Multidisciplinary IR-Tox team	Refined treatment algorithms based on irAE mechanisms

Conroy M, Naidoo J. *Nat Commun* 2022;13(1):392.

Cutaneous adverse events of immune checkpoint inhibitor therapy: incidence and types of reactive dermatoses

Thomas K. Le, Subuhi Kaul, Laura C. Cappelli, Jarushka Naidoo, Yevgeniy R. Semenov & Shawn G. Kwatra

J Dermatolog Treat 2021;23:1-5.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Naidoo

Introduction

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- Dr Gandhi: A 76-year-old woman with epithelioid mesothelioma and disease progression on multiple lines of therapy, including chemotherapy and immunotherapy

MODULE 6: Immunotherapy and Novel Agents in Small Cell Lung Cancer

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Case Presentation: A 76-year-old woman with epithelioid mesothelioma and disease progression on multiple lines of therapy, including chemotherapy and immunotherapy

Dr Sunil Gandhi (Lecanto, Florida)

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- Dr Gupta: A 59-year-old woman with extensive-stage SCLC and PD-L1 TPS 1%

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Case Presentation: A 59-year-old woman with extensive-stage SCLC and PD-L1 TPS 1%

Dr Ranju Gupta (Bethlehem, Pennsylvania)

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In general, what would be your preferred first-line treatment regimen for a 65-year-old patient with extensive-stage small cell lung cancer (SCLC)?

 Dr Aggarwal	Carboplatin/etoposide + atezolizumab	 Dr Hanna	Carboplatin/etoposide + atezolizumab
 Dr Goldberg	Carboplatin/etoposide + atezolizumab	 Dr Liu	Carboplatin/etoposide + atezolizumab
 Dr Govindan	Carboplatin/etoposide + atezolizumab	 Dr Ramalingam	Carboplatin/etoposide + atezolizumab

RTP RESEARCH TO PRACTICE

In what situations if any, do you administer trilaciclib to patients with extensive-stage SCLC who are receiving platinum/etoposide- or topotecan-containing regimens to reduce the incidence of chemotherapy-induced myelosuppression?

 Dr Aggarwal	I do not	 Dr Hanna	I have not yet done so
 Dr Goldberg	Intolerance to G-CSF	 Dr Liu	I have not used trilaciclib but might consider it if multilineage myelosuppression noted with topotecan
 Dr Govindan	None	 Dr Ramalingam	I have not used this in my practice

RTP RESEARCH TO PRACTICE

The benefits and risks of adding durvalumab to platinum/etoposide and of adding atezolizumab to carboplatin/etoposide are very similar, and from a clinical point of view selecting between the 2 regimens as first-line treatment for a patient with extensive-stage SCLC can be considered a “coin flip.”

 Dr Aggarwal	Agree	 Dr Hanna	Agree
 Dr Goldberg	Agree	 Dr Liu	Agree
 Dr Govindan	Agree	 Dr Ramalingam	Agree

RTP RESEARCH TO PRACTICE

In general, what is your preferred second-line treatment for a patient with extensive-stage SCLC with metastases and disease progression on chemotherapy/atezolizumab?

 Dr Aggarwal	Lurbinectedin	 Dr Hanna	Lurbinectedin
 Dr Goldberg	Lurbinectedin	 Dr Liu	Lurbinectedin
 Dr Govindan	Topotecan or irinotecan	 Dr Ramalingam	Lurbinectedin

Appendix

Recent Advances in Adjuvant Systemic Treatment of Solid Tumors

Disease	Agent or regimen			
NSCLC	Atezolizumab (10-15-21)	Osimertinib (12-18-20)	Durvalumab (2-16-18)	Nivolumab/chemotherapy*
Breast	Abemaciclib (10-13-21)	Olaparib	Pembrolizumab (7-26-21)	T-DM1 (5-3-19)
Upper GI	Nivolumab (5-20-21)			
RCC	Pembrolizumab (11-17-21)			
Bladder	Nivolumab (8-19-21)	Pembrolizumab† (1-8-2020)		
Ovarian	Olaparib/bevacizumab (5-8-20)	Niraparib (4-29-20)	Olaparib (12-19-18)	
Melanoma	Dabrafenib/trametinib (4-30-18)	Pembrolizumab (2-15-19)	Nivolumab (12-20-17)	
Prostate	Abiraterone (+ LHRH agonist)			

* Neoadjuvant therapy

† Indicated for patients with non-muscle-invasive bladder cancer who are not eligible for cystectomy but who may have undergone TURBT

RTP RESEARCH TO PRACTICE

FDA Approves Atezolizumab as Adjuvant Treatment for NSCLC

Press Release – October 15, 2021

"The Food and Drug Administration approved atezolizumab for adjuvant treatment following resection and platinum-based chemotherapy in patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test.

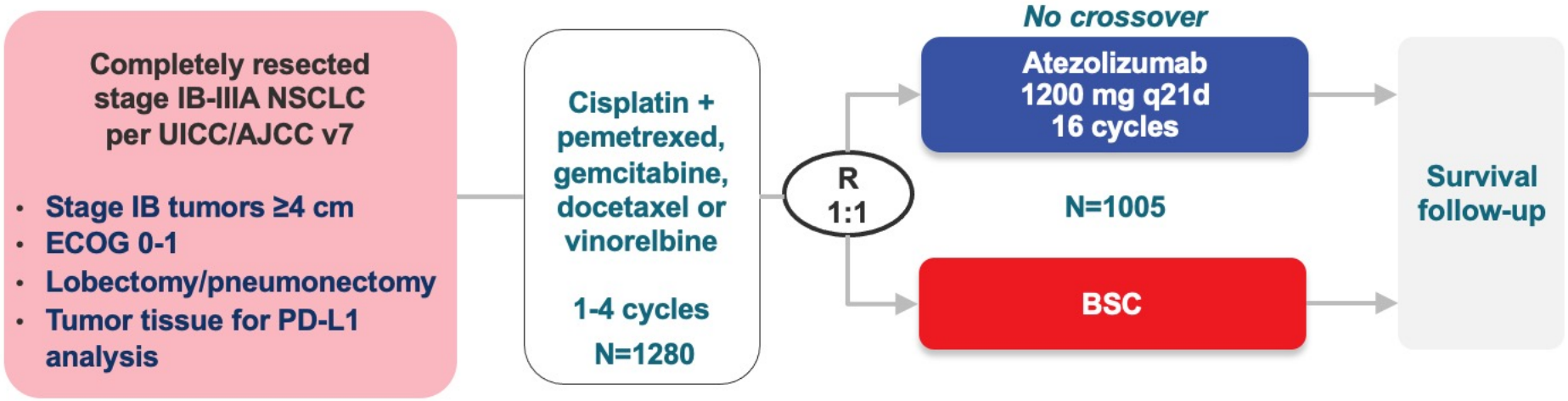
Today, the FDA also approved the VENTANA PD-L1 (SP263) Assay (Ventana Medical Systems, Inc.) as a companion diagnostic device to select patients with NSCLC for adjuvant treatment with atezolizumab.

The major efficacy outcome measure was disease-free survival (DFS) as assessed by the investigator in the primary efficacy analysis population (n=476) of patients with stage II-IIIA NSCLC with PD-L1 expression on ≥1% of tumor cells (PD-L1 ≥1% TC). Median DFS was not reached (95% CI: 36.1, NE) in patients on the atezolizumab arm compared with 35.3 months (95% CI: 29.0, NE) on the BSC arm (HR 0.66; 95% CI: 0.50, 0.88; p=0.004)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-atezolizumab-adjuvant-treatment-non-small-cell-lung-cancer

RTP RESEARCH TO PRACTICE

IMpower010: A Phase III Trial of Adjuvant Atezolizumab After Chemotherapy for Resected Stage IB-IIIA NSCLC



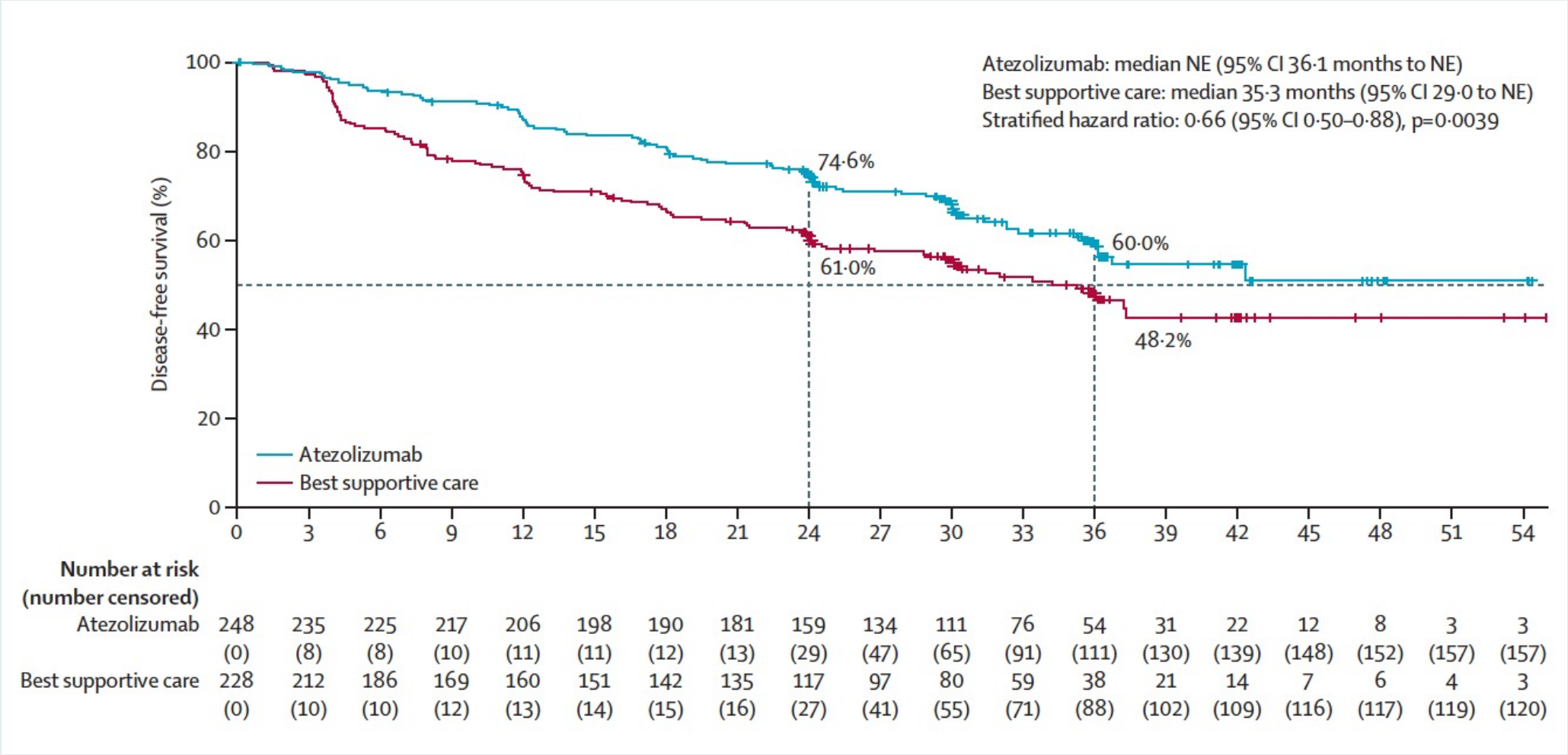
Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

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)**

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

Wakelee HA et al. ASCO 2021;Abstract 8500.

IMpower010 Primary Endpoint: Disease-Free Survival in the PD-L1 ≥1% Tumor Cells Stage II-IIIA Population



Felip E et al. *Lancet* 2021;398(10308):1344-57.

IMpower010: Efficacy Summary

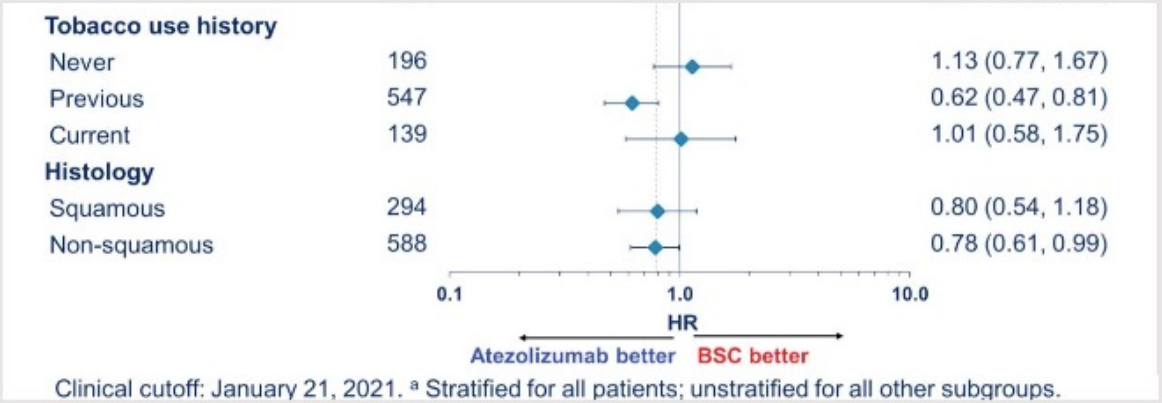
	Atezolizumab	BSC	HR (*p*-value)
TC PD-L1 ≥1%, Stage II-IIIA (n = 248, 228)			
Median disease-free survival (DFS)	Not estimable	35.3 mo	0.66 (0.0039)
2-year DFS rate	75%	61%	-
3-year DFS rate	60%	48%	-
All randomized Stage II-IIIA (n = 442, 440)			
Median DFS	42.3 mo	35.3 mo	0.79 (0.020)
2-year DFS rate	70%	62%	-
3-year DFS rate	56%	50%	-
ITT population (n = 507, 598)			
Median DFS	Not estimable	37 mo	0.81 (0.040)
2-year DFS rate	71%	64%	-
3-year DFS rate	58%	53%	-

BSC = best supportive care; TC = tumor cells

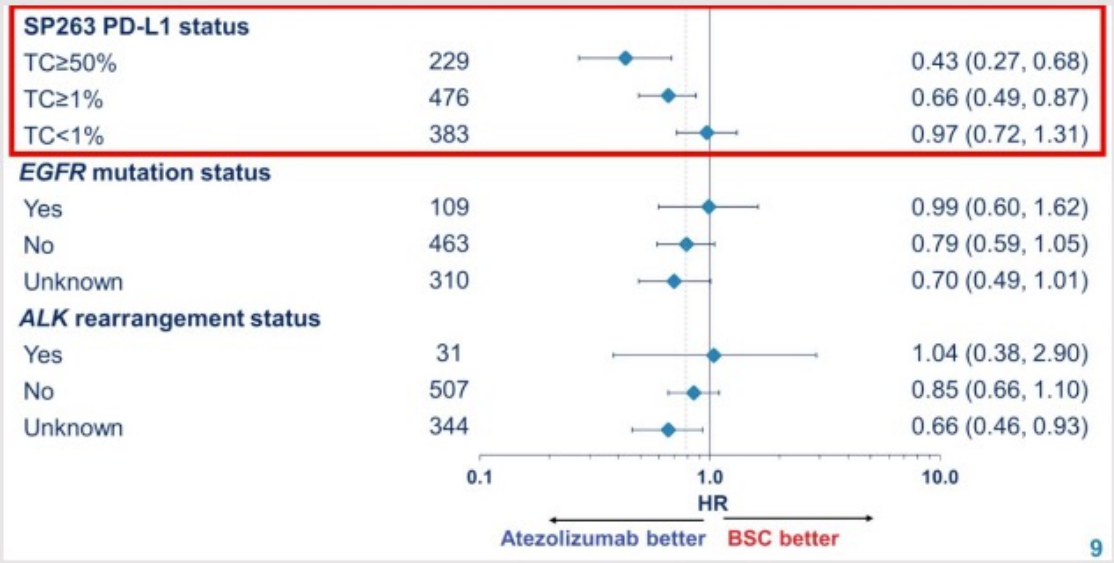
Overall survival data in the ITT population were immature and not formally tested.

Felip E et al. *Lancet* 2021;398(10308):1344-57.

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

RTP RESEARCH TO PRACTICE

IMpower010: Safety Summary

	Atezolizumab group (n=495)	Best supportive care group (n=495)
Adverse event		
Any grade	459 (93%)	350 (71%)
Grade 3–4	108 (22%)	57 (12%)
Serious	87 (18%)	42 (8%)
Grade 5	8 (2%)*	3 (1%)†
Led to dose interruption of atezolizumab	142 (29%)	..
Led to atezolizumab discontinuation	90 (18%)	..
Immune-mediated adverse events		
Any grade	256 (52%)	47 (9%)
Grade 3–4	39 (8%)	3 (1%)
Required the use of systemic corticosteroids‡	60 (12%)	4 (1%)
Led to discontinuation	52 (11%)	0

Data are n (%). *Interstitial lung disease, multiple organ dysfunction syndrome, myocarditis, and acute myeloid leukaemia (all four events related to atezolizumab), and pneumothorax, cerebrovascular accident, arrhythmia, and acute cardiac failure. †Pneumonia; pulmonary embolism; and cardiac tamponade and septic shock in the same patient. ‡Atezolizumab-related.

Felip E et al. *Lancet* 2021;398(10308):1344-57.

RTP RESEARCH TO PRACTICE

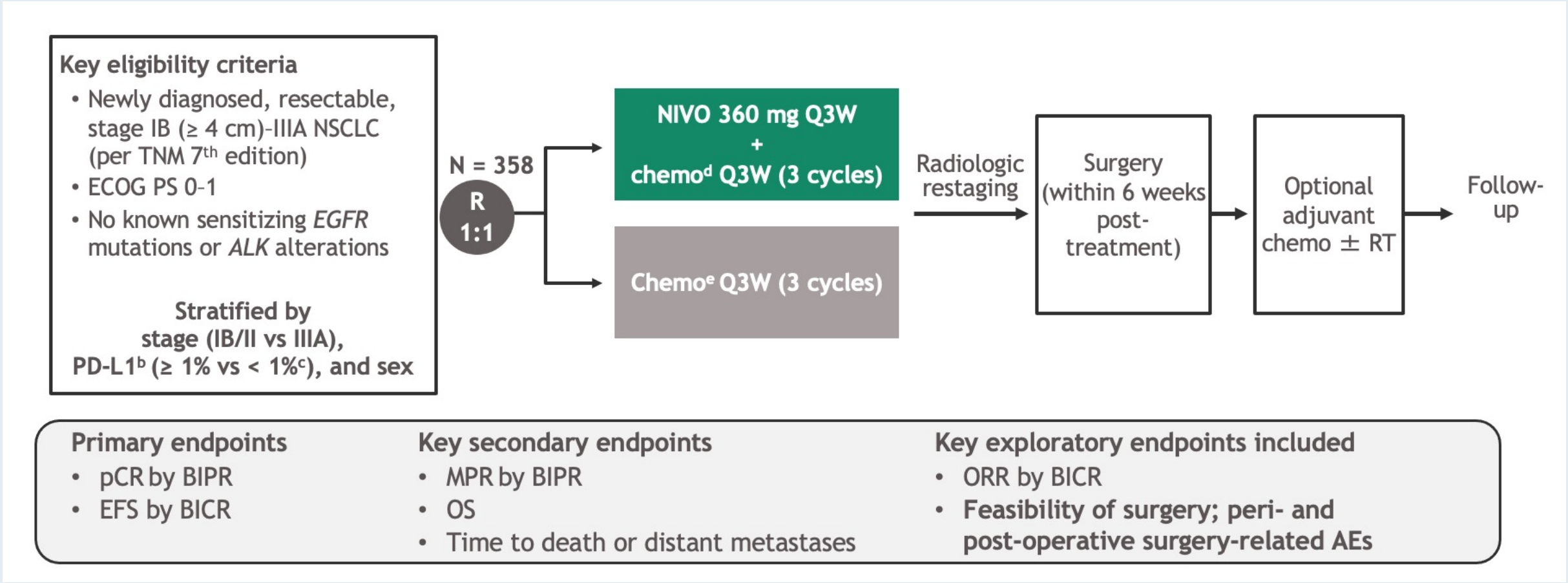
CheckMate 816 Met a Primary Endpoint of Improved Event-Free Survival with Neoadjuvant Nivolumab in Combination with Chemotherapy

Press Release: November 8, 2021

"The Phase 3 CheckMate-816 trial met the primary endpoint of improved event-free survival (EFS) in patients with resectable stage IB to IIIA non-small cell lung cancer (NSCLC). In a prespecified interim analysis, nivolumab plus chemotherapy showed a statistically significant and clinically meaningful improvement in EFS compared to chemotherapy alone when given before surgery. This combination previously showed a significant improvement of pathologic complete response (pCR), the trial's other primary endpoint. The safety profile of nivolumab plus chemotherapy was consistent with previously reported studies in NSCLC. CheckMate-816 is the first Phase 3 trial with an immunotherapy-based combination to demonstrate a statistically significant and clinically meaningful benefit as a neoadjuvant treatment for patients with non-metastatic non-small cell lung cancer."

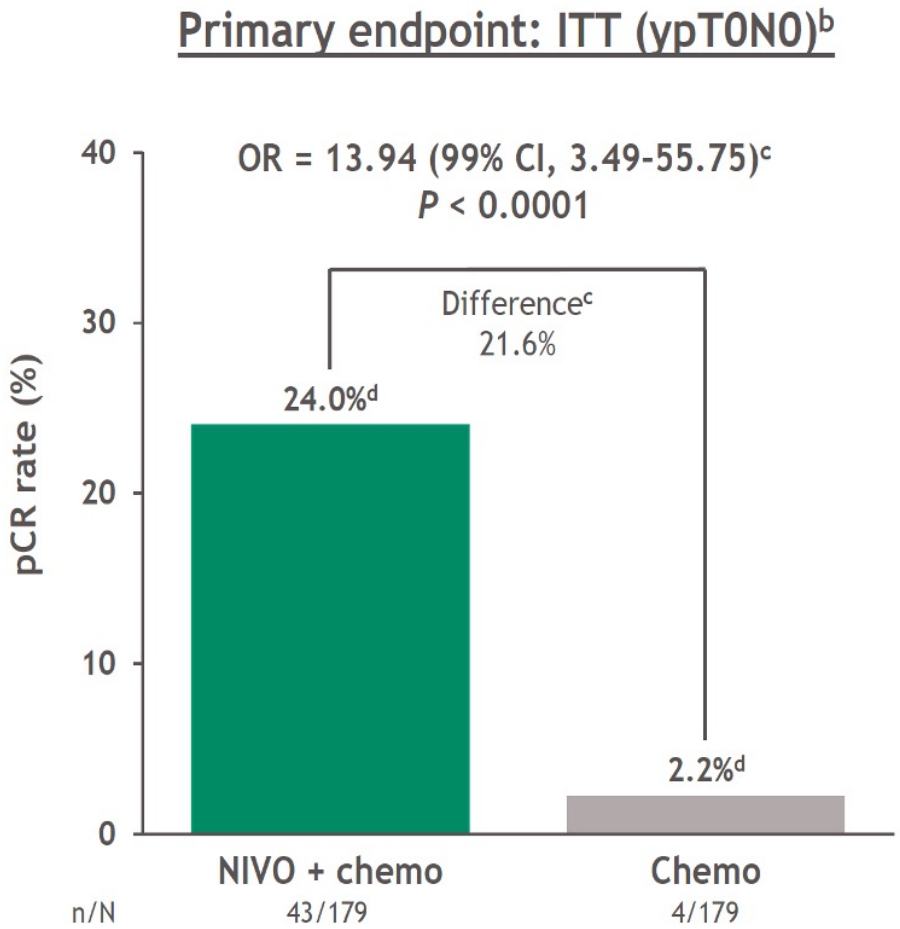
https://news.bms.com/news/details/2021/Neoadjuvant-Opdivo-nivolumab-Plus-Chemotherapy-Significantly-Improves-Event-Free-Survival-in-Patients-with-Resectable-Non-Small-Cell-Lung-Cancer-in-Phase-3-CheckMate--816-Trial/default.aspx

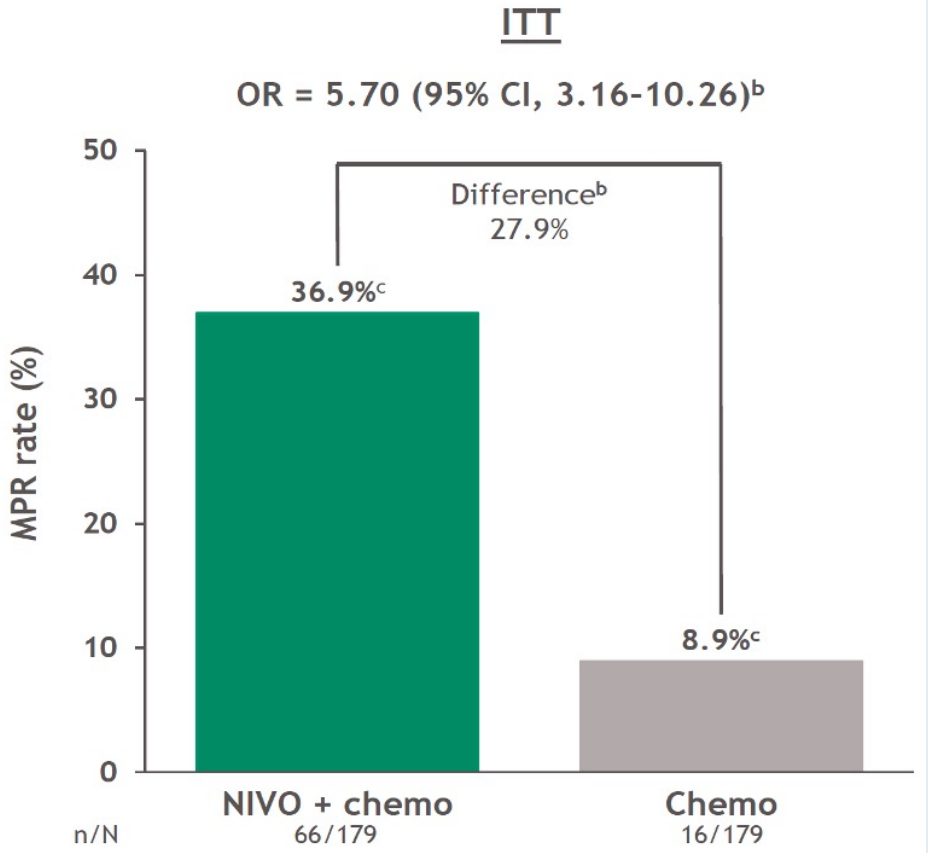
CheckMate 816: A Phase III Trial of Neoadjuvant Nivolumab with Chemotherapy for Newly Diagnosed, Resectable, Stage IB-IIIA NSCLC



Spicer J et al. ASCO 2021;Abstract 8503.

CheckMate 816 Coprimary Endpoint: Pathologic Complete Response (pCR)



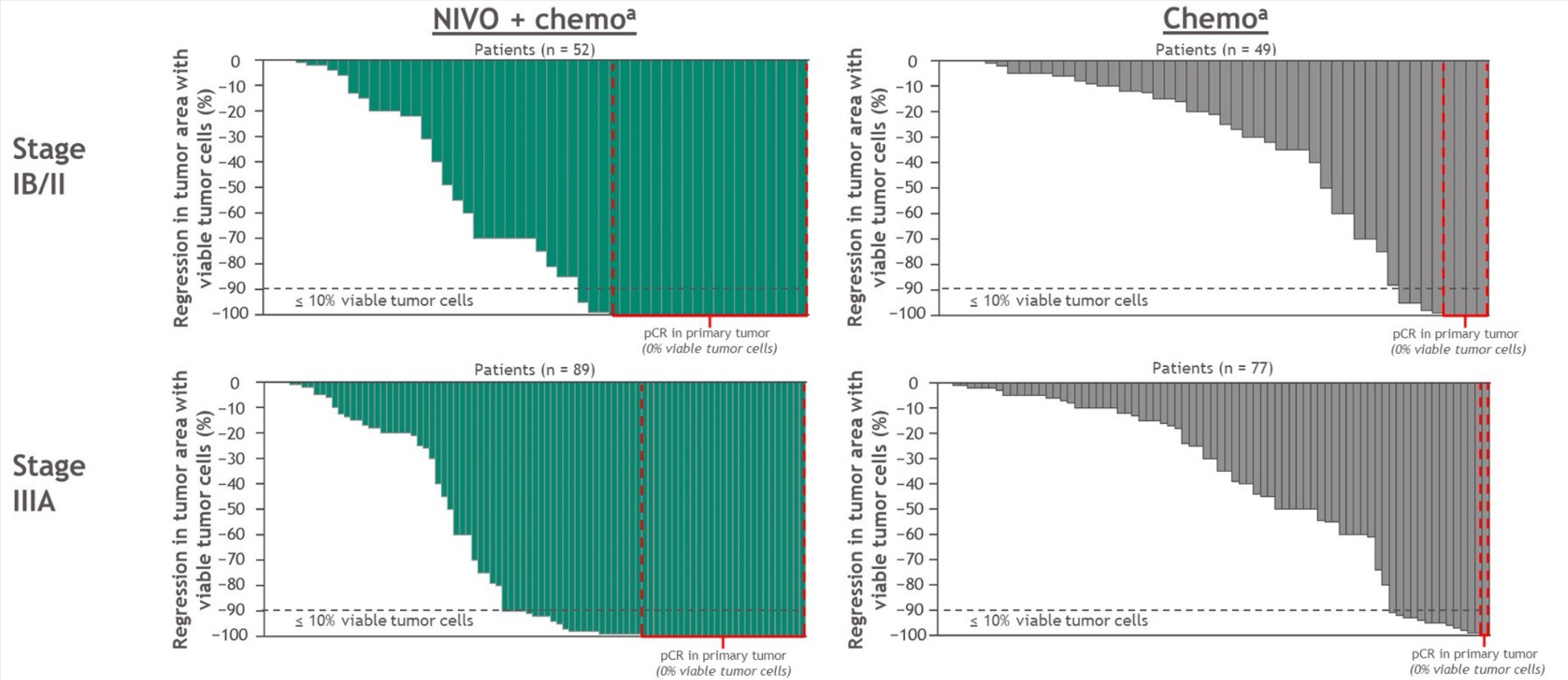


- pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4-29.0)

Forde PM et al. AACR 2021;Abstract CT003.

RTP RESEARCH TO PRACTICE

CheckMate 816: Depth of Pathologic Regression in Primary Tumor by Stage



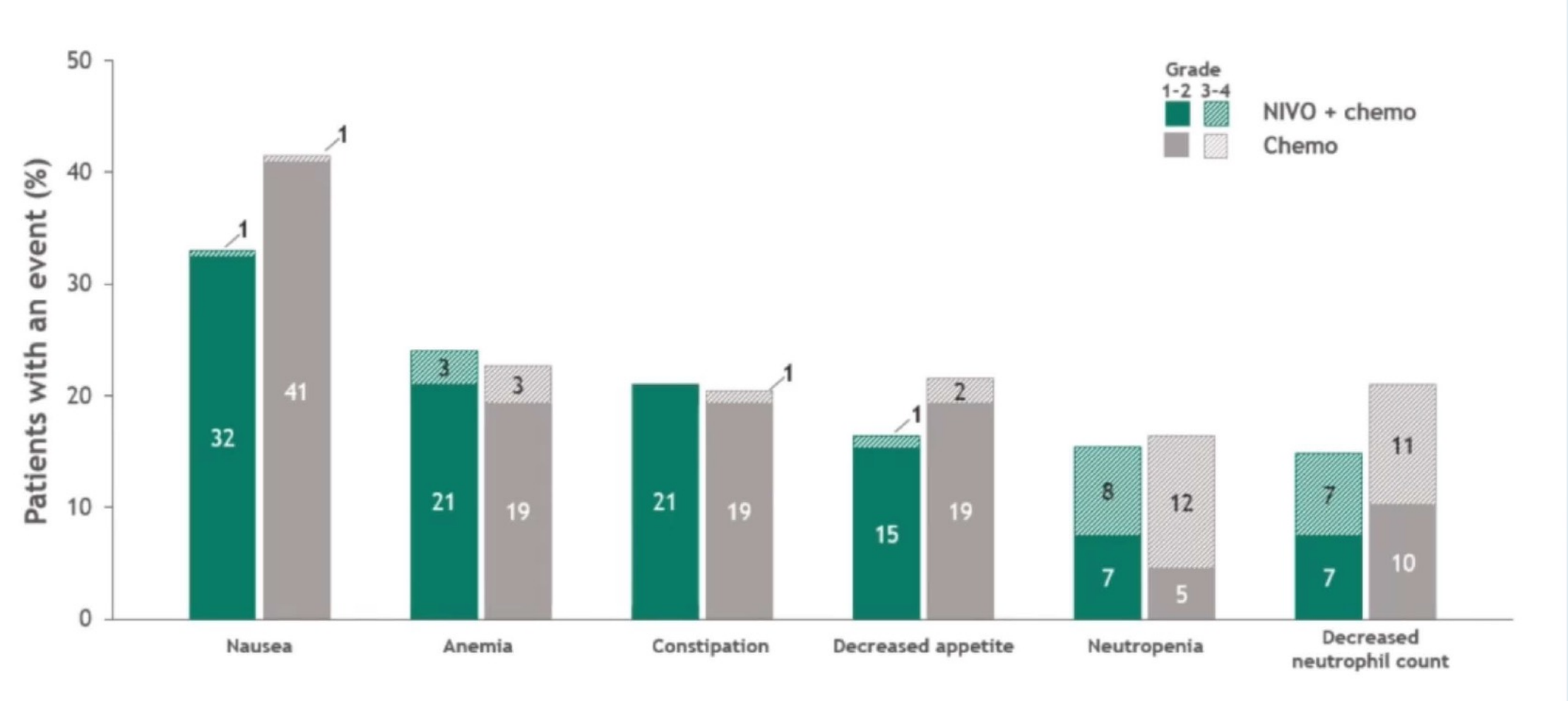
- The median residual viable tumor percentage in stage IB/II and IIIA was 28% and 8% with NIVO + chemo vs 79% and 70% with chemo, respectively

[a]Response-evaluable patients.

Spicer J et al. ASCO 2021;Abstract 8503.

RTP RESEARCH TO PRACTICE

CheckMate 816: Treatment-Related Adverse Events in ≥15% of Patients



Forde PM et al. AACR 2021;Abstract CT003.

Select Ongoing Phase III Trials of Immunotherapy in the Neoadjuvant Setting

Trial identifier	N	Patient population	Study arms
IMpower030 (NCT03456063)	453	Resectable Stage II, IIIA or select IIIB (T3N2 only) NSCLC Squamous or nonsquamous histology	• Atezolizumab + platinum-based chemotherapy • Placebo + platinum-based chemotherapy
KEYNOTE-671 (NCT03425643)	786	Resectable Stage II, IIIA or resectable IIIB (T3-4N2) NSCLC	• Pembrolizumab + platinum-based chemotherapy • Placebo + platinum-based chemotherapy
AEGEAN (NCT03800134)	800	Resectable Stage IIA to select (ie, N2) Stage IIIB NSCLC	• Durvalumab + platinum-based chemotherapy • Placebo + platinum-based chemotherapy

www.clinicaltrials.gov; Accessed November 2021.

Select Ongoing Phase III Trials of Immunotherapy in the Adjuvant Setting

Trial identifier	N	Patient population	Study arms
BR31 (NCT02273375)	1,360	Stage IB (≥4 cm in the longest diameter), II or IIIA after complete resection	• Durvalumab • Placebo
KEYNOTE-091/ PEARLS (NCT02504372)	1,177	Stage IB with T ≥4 cm, II-IIIA NSCLC after complete surgical resection with or without adjuvant chemotherapy	• Pembrolizumab • Placebo
ANVIL (NCT02595944)	903	Complete surgical resection of Stage IB (≥4 cm), II or IIIA NSCLC with adjuvant chemotherapy Negative for ALK translocation and EGFR exon 19 deletion or exon 21 L858R mutation	• Nivolumab • Placebo

www.clinicaltrials.gov; Accessed November 2021.

Stage III NSCLC

ASCO special articles

Management of Stage III Non–Small-Cell Lung Cancer: ASCO Guideline

Megan E. Daly, MD[1]; Navneet Singh, MD, DM[2]; Nofisat Ismaila, MD, MSc[3]; Mara B. Antonoff, MD[4]; Douglas A. Arenberg, MD[5]; Jeffrey Bradley, MD[6]; Elizabeth David, MD[7]; Frank Detterbeck, MD[8]; Martin Früh, MD[9,10]; Matthew A. Gubens, MD, MS[11]; Amy C. Moore, PhD[12]; Sukhmani K. Padda, MD[13]; Jyoti D. Patel, MD[14]; Tanyanika Phillips, MD, MPH[15]; Angel Qin, MD[5]; Clifford Robinson, MD[16]; and Charles B. Simone II, MD[17]

J Clin Oncol 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

original reports

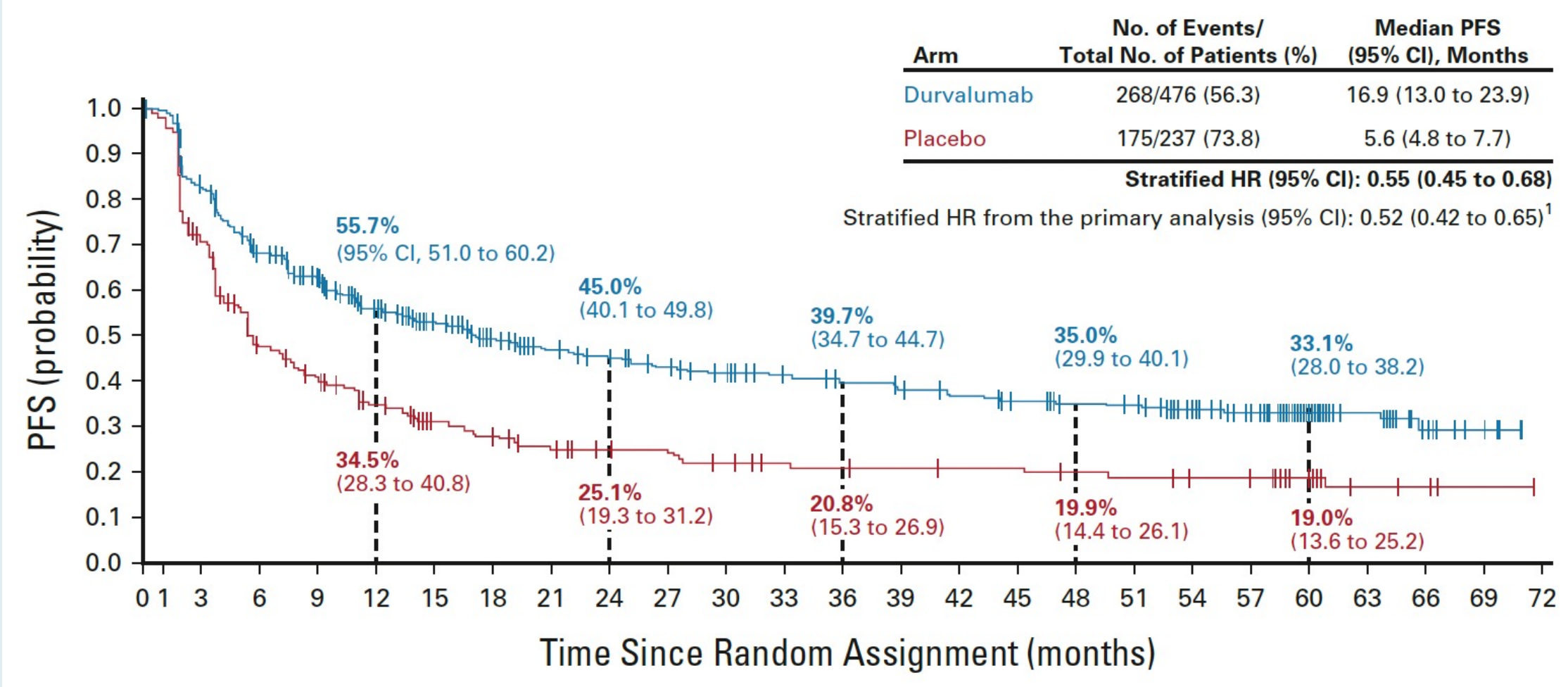
Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

David R. Spigel, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Jhanelle E. Gray, MD[3]; David Vicente, MD[4]; David Planchard, MD, PhD[5]; Luis Paz-Ares, MD, PhD[6]; Johan F. Vansteenkiste, MD, PhD[7]; Marina C. Garassino, MD[8,9]; Rina Hui, PhD[10]; Xavier Quantin, MD, PhD[11]; Andreas Rimner, MD[12]; Yi-Long Wu, MD[13]; Mustafa Özgüroğlu, MD[14]; Ki H. Lee, MD[15]; Terufumi Kato, MD[16]; Maike de Wit, MD, PhD[17]; Takayasu Kurata, MD[18]; Martin Reck, MD, PhD[19]; Byoung C. Cho, MD, PhD[20]; Suresh Senan, PhD[21]; Jarushka Naidoo, MBBCH, MHS[22]; Helen Mann, MSc[23]; Michael Newton, PharmD[24]; Piruntha Thiyagarajah, MD[23]; and Scott J. Antonia, MD, PhD[3]; on behalf of the PACIFIC Investigators

J Clin Oncol 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

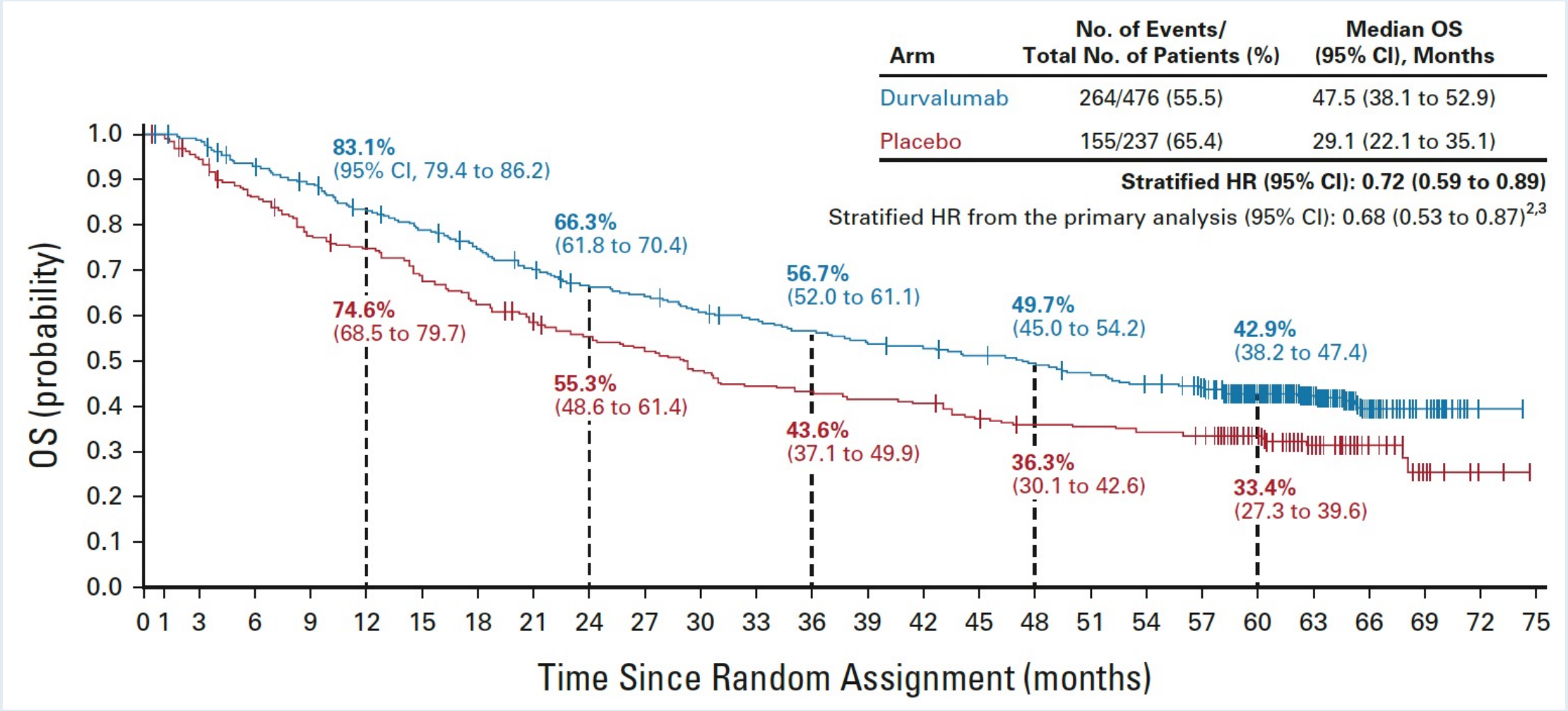
PACIFIC: Five-Year Progression-Free Survival (PFS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

PACIFIC: Five-Year Overall Survival (OS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

PACIFIC-R: Real-World Study of Durvalumab After Chemoradiation Therapy for Patients with Unresectable Stage III NSCLC

- International observational study (N = 1,155)
- Median PFS: 22.5 months
- Median duration of durvalumab treatment: 11 months

Summary of safety and pneumonitis	N = 1,155
Discontinuation of durvalumab due to AE	17.5%
Discontinuation of durvalumab due to pneumonitis Temporary Permanent	13.8% 5.1% 8.7%
Any-grade pneumonitis and/or interstitial lung disease Moderate severity Life-threatening Fatal	18.5% 8.8% 0.2% 0.1%

Girard N et al. ESMO 2021;Abstract 1171MO.

RTP RESEARCH TO PRACTICE

FDA Approves Durvalumab for Fixed-Dose Use in NSCLC, Bladder Cancer Indications

Press Release: November 20, 2020

"The FDA has approved durvalumab for an additional dosing option, a fixed dose of 1500 mg every 4 weeks, in the approved indications of unresectable stage III non-small cell lung cancer after chemoradiation and previously treated advanced bladder cancer.

This new dosing option is consistent with the dosing for the agent that has been approved in extensive-stage small cell lung cancer (ES-SCLC); this will serve as an alternative option for patients who weigh more than 30 kg rather than the weight-based dosing of 10 mg/kg that is administered every 2 weeks.

The regulatory decision was based on data from several clinical trials examining the agent, including the phase 3 PACIFIC trial (NCT02125461), which supported the 2-week, weight-based dosing in patients with unresectable stage III NSCLC, and the phase 3 CASPIAN trial (NCT03043872), which examined a 4-week, fixed-dose during maintenance treatment in patients with ES-SCLC."

https://www.onclive.com/view/fda-approves-durvalumab-for-fixed-dose-use-in-nsclc-bladder-cancer-indications

RTP RESEARCH TO PRACTICE

Phase II KEYNOTE-799 Trial of Pembrolizumab with Concurrent Chemoradiation Therapy for Unresectable Stage III NSCLC

Coprimary Endpoints: Overall Response Rate (ORR) and Grade 3 or Higher Pneumonitis

	Cohort A (squamous and nonsquamous) (n = 112)	Cohort B (nonsquamous only) (n = 102)
ORR	70.5%	70.6%
12-month PFS	67.1%	71.6%
12-month OS	81.3%	87.0%
Grade ≥3 pneumonitis	8.0%	6.9%

Jabbour SK et al. *IJROBP* 2021;11(3, Suppl):9-10.

RTP RESEARCH TO PRACTICE

First-Line Therapy for Metastatic NSCLC

FDA-Approved Immunotherapy Combination Options for First-Line Therapy

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab (q3wk or q6wk) + Platinum and pemetrexed[1]	8/20/18	KEYNOTE-189	Nonsquamous	0.56
Pembrolizumab (q3wk or q6wk) + Carboplatin, paclitaxel or *nab* paclitaxel[2]	10/30/18	KEYNOTE-407	Squamous	0.71
Atezolizumab (q3wk) + Carboplatin and paclitaxel and bevacizumab[3]	12/6/18	IMpower150	Nonsquamous	0.80
Atezolizumab (q3wk) + Carboplatin and *nab* paclitaxel[4]	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab (q2wk) + Ipilimumab[5]	5/15/20	CheckMate 227	PD-L1 TPS ≥1, EGFR and/or ALK wt	0.76
Nivolumab (q3wk) + Ipilimumab and chemotherapy[6]	5/26/20	CheckMate 9LA	EGFR and/or ALK wt	0.72

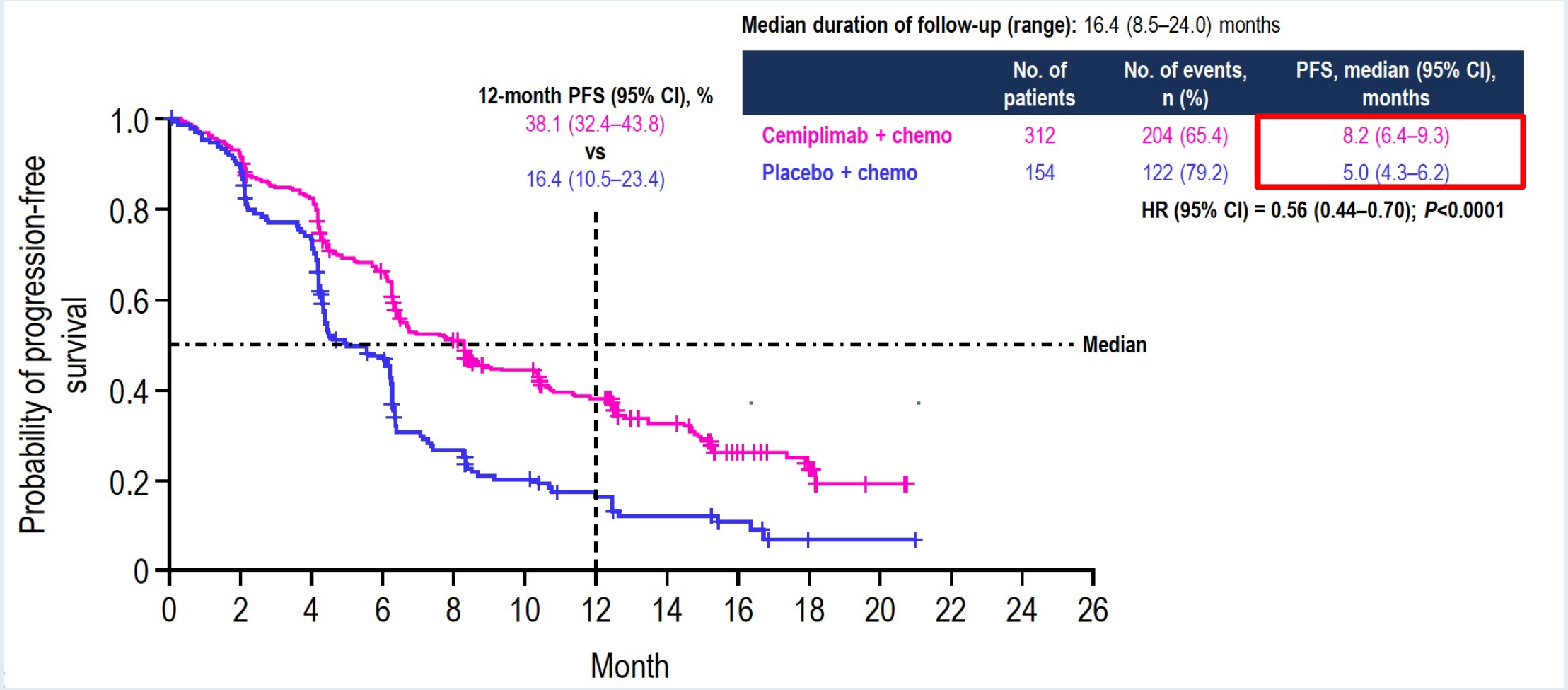
[1] Rodriguez-Abreu. *Ann Oncol* 2021. [2] Paz-Ares. *J Thorac Oncol* 2020. [3] Socinski *J Thorac Oncol* 2021. [4] West. *Lancet Oncol* 2019.
[5] Paz-Ares. ASCO 2021;Abstract 9016. [6] Reck. ASCO 2021;Abstract 9000.

EMPOWER-Lung 3: Progression-Free Survival

Median duration of follow-up (range): 16.4 (8.5–24.0) months

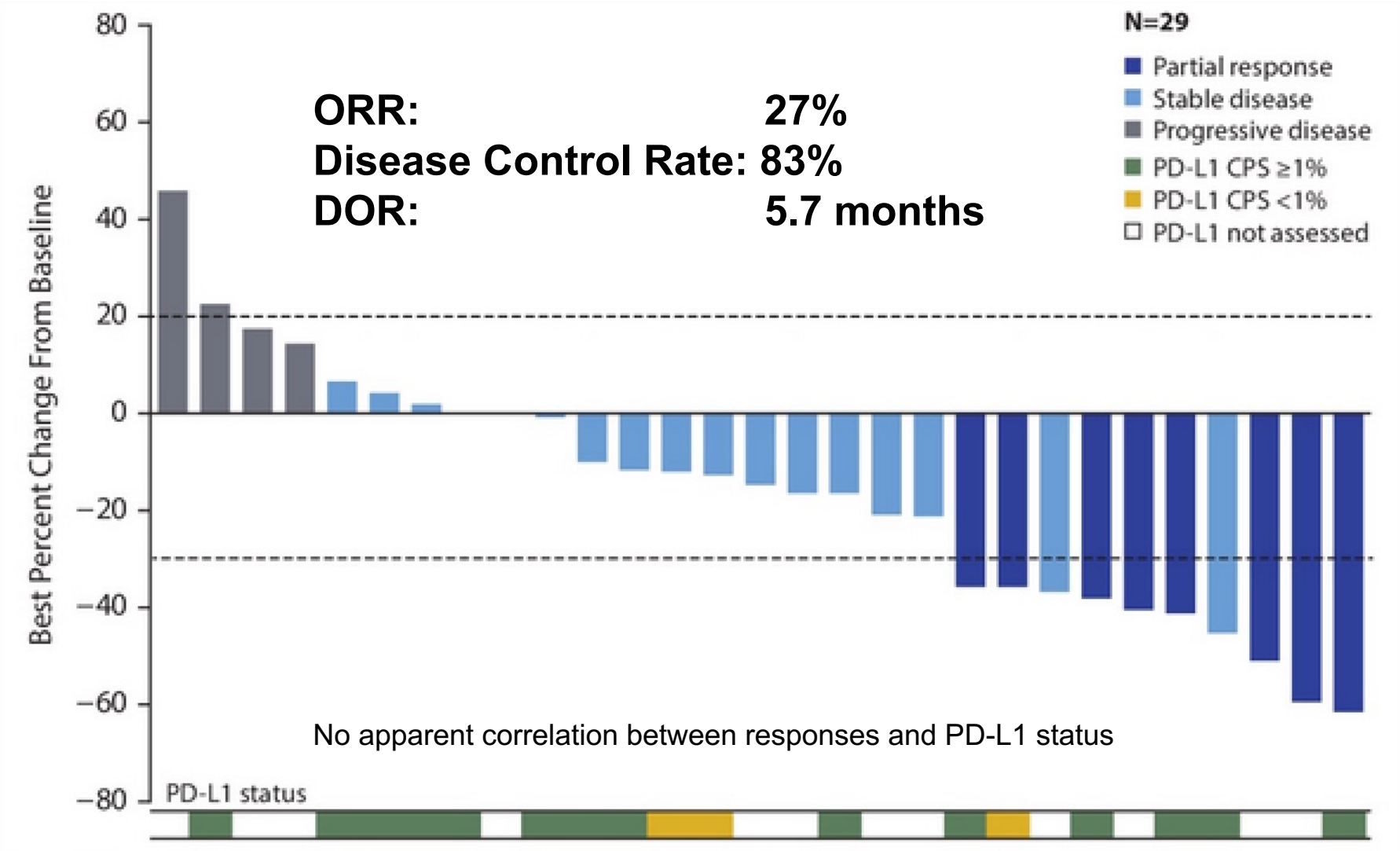
	No. of patients	No. of events, n (%)	PFS, median (95% CI), months
Cemiplimab + chemo	312	204 (65.4)	8.2 (6.4–9.3)
Placebo + chemo	154	122 (79.2)	5.0 (4.3–6.2)

HR (95% CI) = 0.56 (0.44–0.70); *P*<0.0001



Gogishvili M et al. ESMO 2021;Abstract LBA51.

COSMIC-021 (Cohort 7): Best Change from Baseline with Cabozantinib/Atezolizumab for Metastatic NSCLC



Patient population

- Radiographic progression on or after 1 prior ICI treatment
- ≤2 lines of prior systemic anticancer therapy for metastatic NSCLC
- No EGFR mutations, ALK or ROS1 rearrangements or BRAF V600E mutation

Neal JW et al. ASCO 2020;Abstract 9610.

RTP RESEARCH TO PRACTICE

COSMIC-021 (Cohort 7): Immune-Related Adverse Events with Cabozantinib/Atezolizumab for Metastatic NSCLC

	NSCLC Cohort 7 (N=30)	
	Any Grade	Grade 3
Any AE, n (%)	6 (20)	0
Hyperthyroidism	1 (3.3)	0
Hypothyroidism	1 (3.3)	0
Lipase increased	1 (3.3)	0
Myocarditis*	1 (3.3)	0
Pain	1 (3.3)	0
Pneumonitis*	1 (3.3)	0
Rash	1 (3.3)	0

*One patient experienced grade 5 pneumonitis and myocarditis; pneumonitis was assessed as the cause of death

Neal JW et al. ASCO 2020;Abstract 9610.

Enrollment Complete in Phase III CONTACT-01 Pivotal Trial of Cabozantinib in Combination with an Immune Checkpoint Inhibitor for Previously Treated Metastatic NSCLC

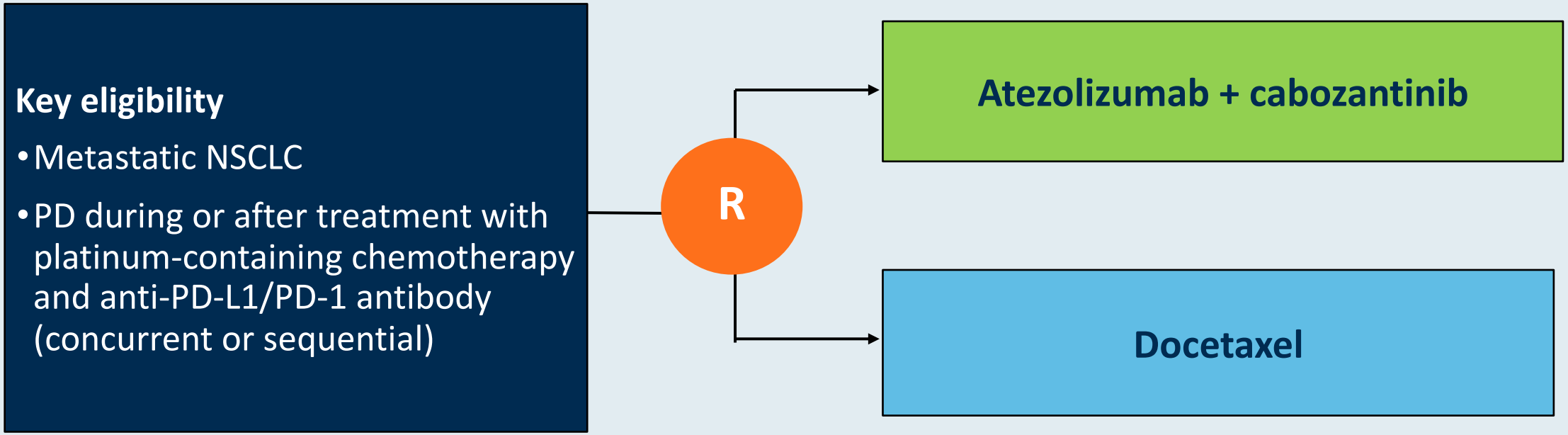
Press Release: November 9, 2021

"Enrollment is now completed for CONTACT-01, the global, phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab in patients with metastatic non-small cell lung cancer (NSCLC) who have been previously treated with an immune checkpoint inhibitor and platinum-containing chemotherapy.

CONTACT-01 is a global, multicenter, randomized, phase 3, open-label study that enrolled 366 patients who were randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of docetaxel. The primary endpoint of the trial is overall survival. Secondary endpoints include progression-free survival, objective response rate and duration of response. Results from cohort 7 of the phase 1b COSMIC-021 trial informed the CONTACT-01 trial design."

https://ir.exelixis.com/news-releases/news-release-details/exelixis-announces-enrollment-completion-phase-3-contact-01

CONTACT-01 Phase III Study Design



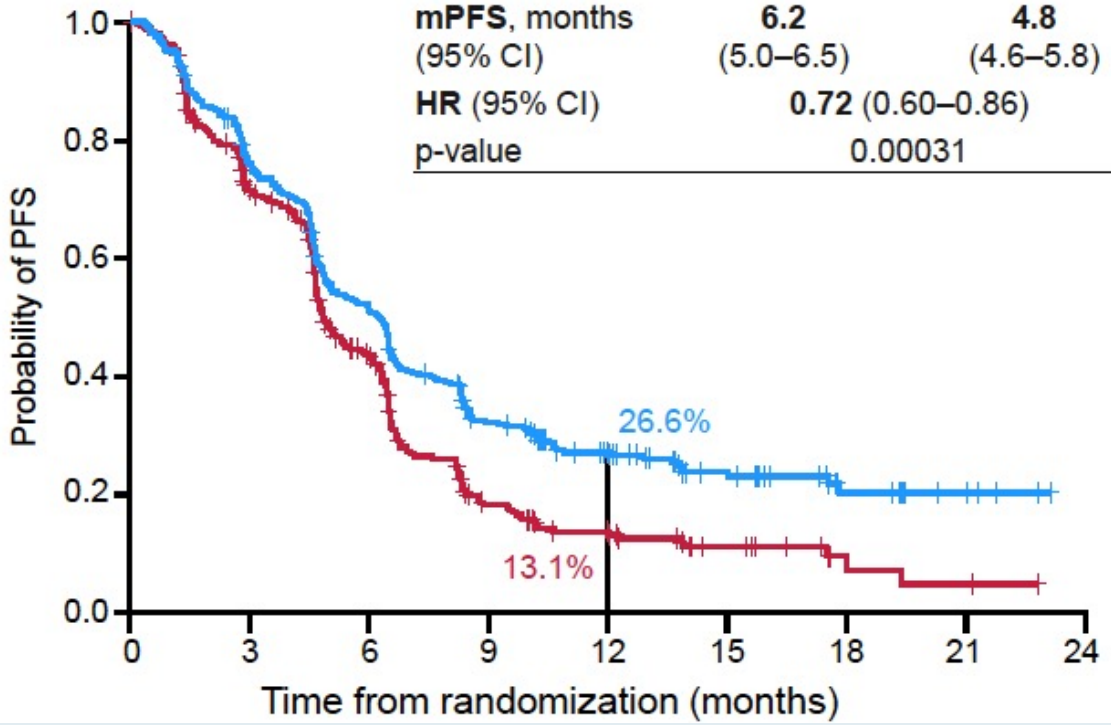
Primary endpoint: Overall survival
Secondary endpoints: PFS, ORR, DOR, others

www.clinicaltrials.gov. NCT04471428. Accessed November 2021.

POSEIDON: First-Line Durvalumab with Tremelimumab and Chemotherapy for Advanced NSCLC

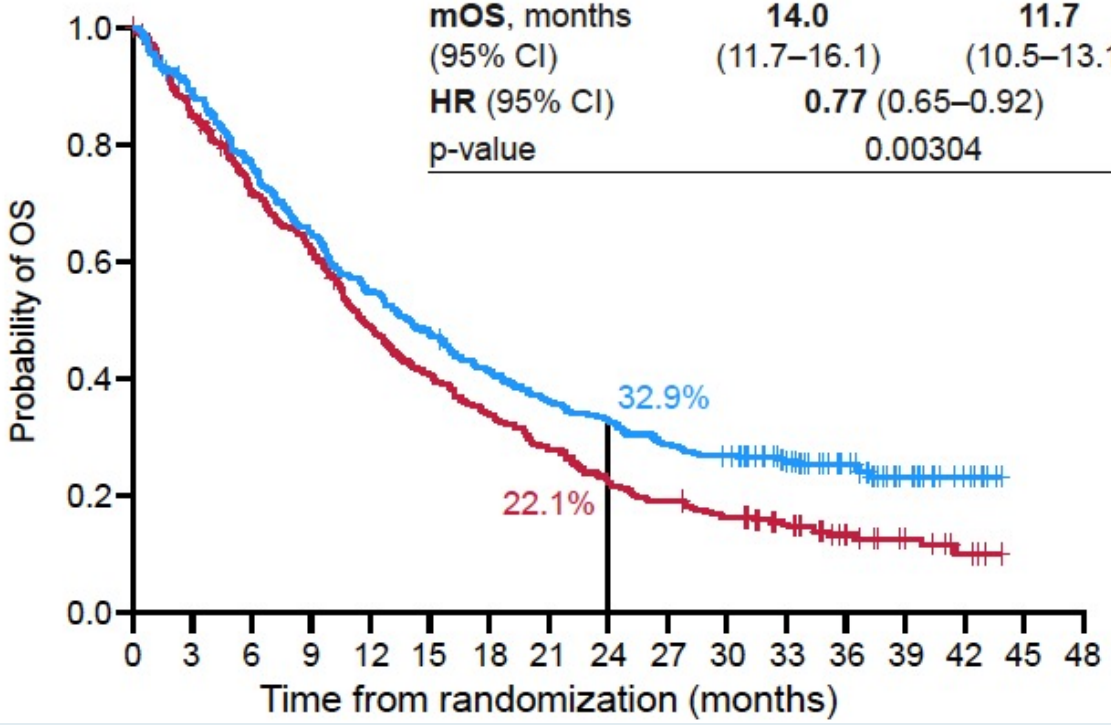
PFS

	D+T+CT	CT
Events, n/N (%)	238/338 (70.4)	258/337 (76.6)
mPFS, months (95% CI)	**6.2** (5.0–6.5)	**4.8** (4.6–5.8)
HR (95% CI)	**0.72** (0.60–0.86)	
p-value	0.00031	



OS

	D+T+CT	CT
Events, n/N (%)	251/338 (74.3)	285/337 (84.6)
mOS, months (95% CI)	**14.0** (11.7–16.1)	**11.7** (10.5–13.1)
HR (95% CI)	**0.77** (0.65–0.92)	
p-value	0.00304	



Johnson ML et al. WCLC 2021;Abstract PL02.01

RTP RESEARCH TO PRACTICE

Background: TIGIT Pathway

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a novel inhibitory receptor expressed on multiple immune cells, including T cells and NK cells[1-3]
- TIGIT inhibits T cells and NK cells by binding to its ligand PVR on tumor cells and antigen-presenting cells (APCs)
- TIGIT expression strongly correlates with PD-1 expression, especially in tumor-infiltrating T cells in lung cancer
- *Hypothesis*: Anti-TIGIT antibodies, which prevent TIGIT from binding to its ligand, could restore the anti-tumor response and could complement the activity of anti-PD-L1/PD-1 antibodies

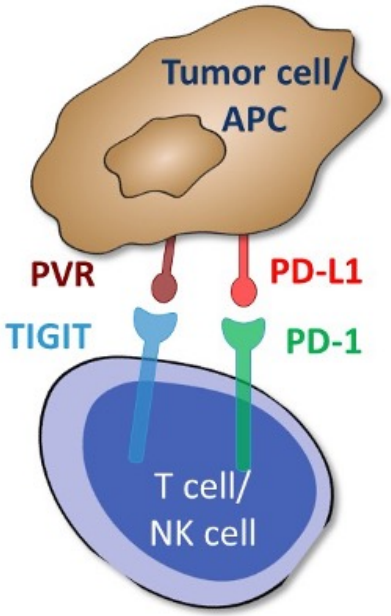


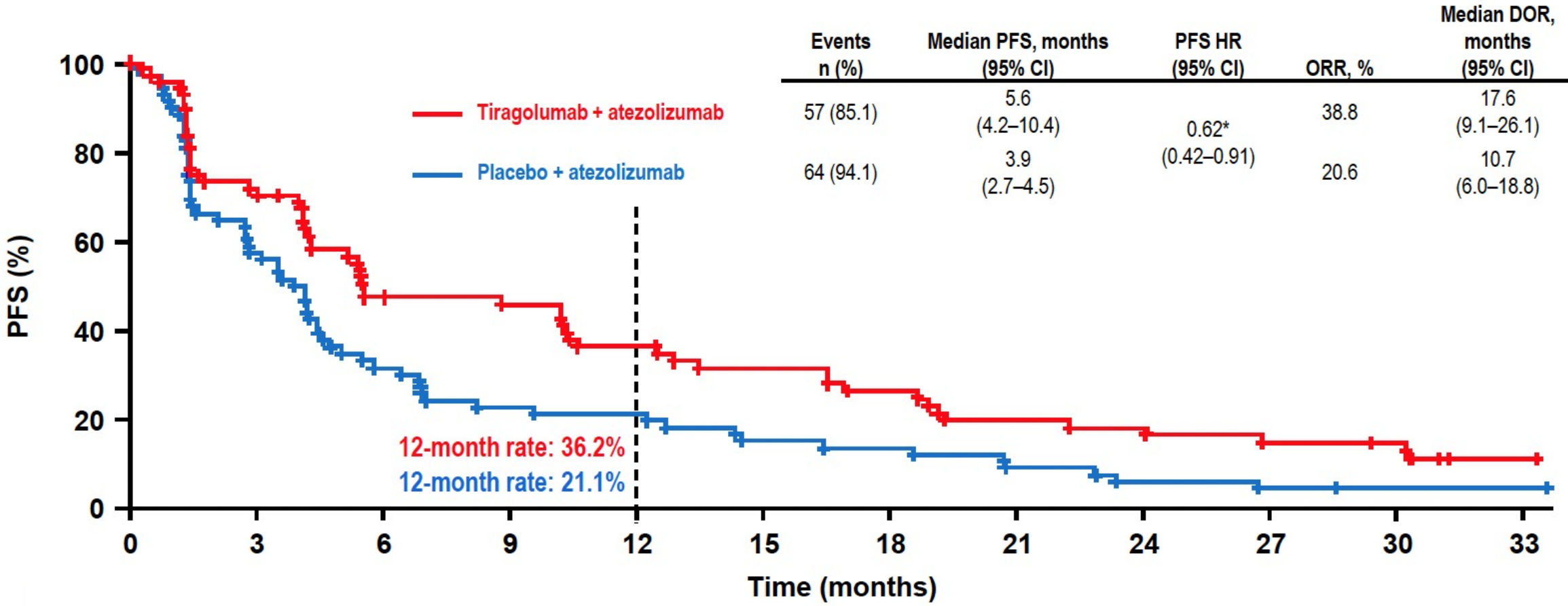
Figure adapted from Manieri et al. *Trends Immunology* 2017

NK, natural killer; PVR, poliovirus receptor

[1] Manieri et al. *Trends Immunology* 2017; [2] Rotte et al. *Annals of Oncology* 2018; [3] Yu et al. *Nature Immunology* 2009

Rodriguez-Abreu D et al. ASCO 2020;Abstract 9503.

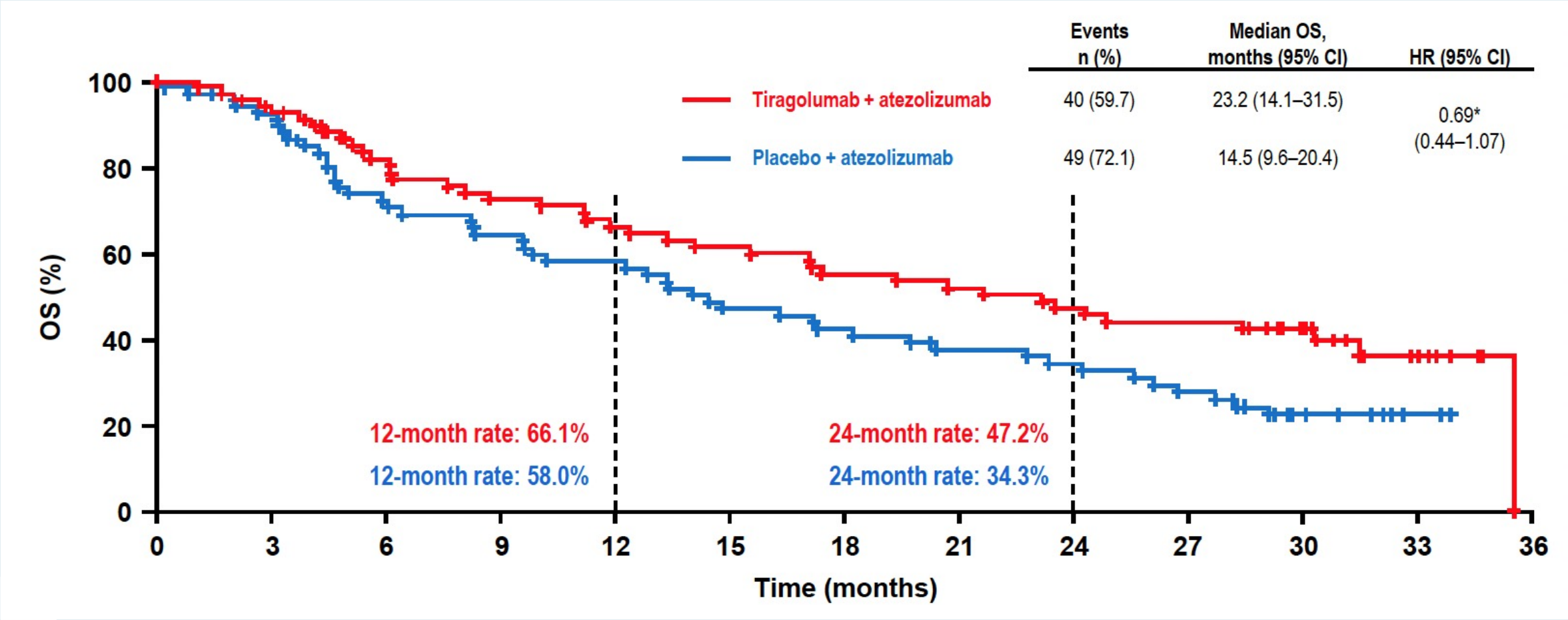
CITYSCAPE: Investigator-Assessed PFS (ITT)



	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tiragolumab + atezolizumab	57 (85.1)	5.6 (4.2–10.4)	0.62* (0.42–0.91)	38.8	17.6 (9.1–26.1)
Placebo + atezolizumab	64 (94.1)	3.9 (2.7–4.5)		20.6	10.7 (6.0–18.8)

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Investigator-Assessed OS (ITT)



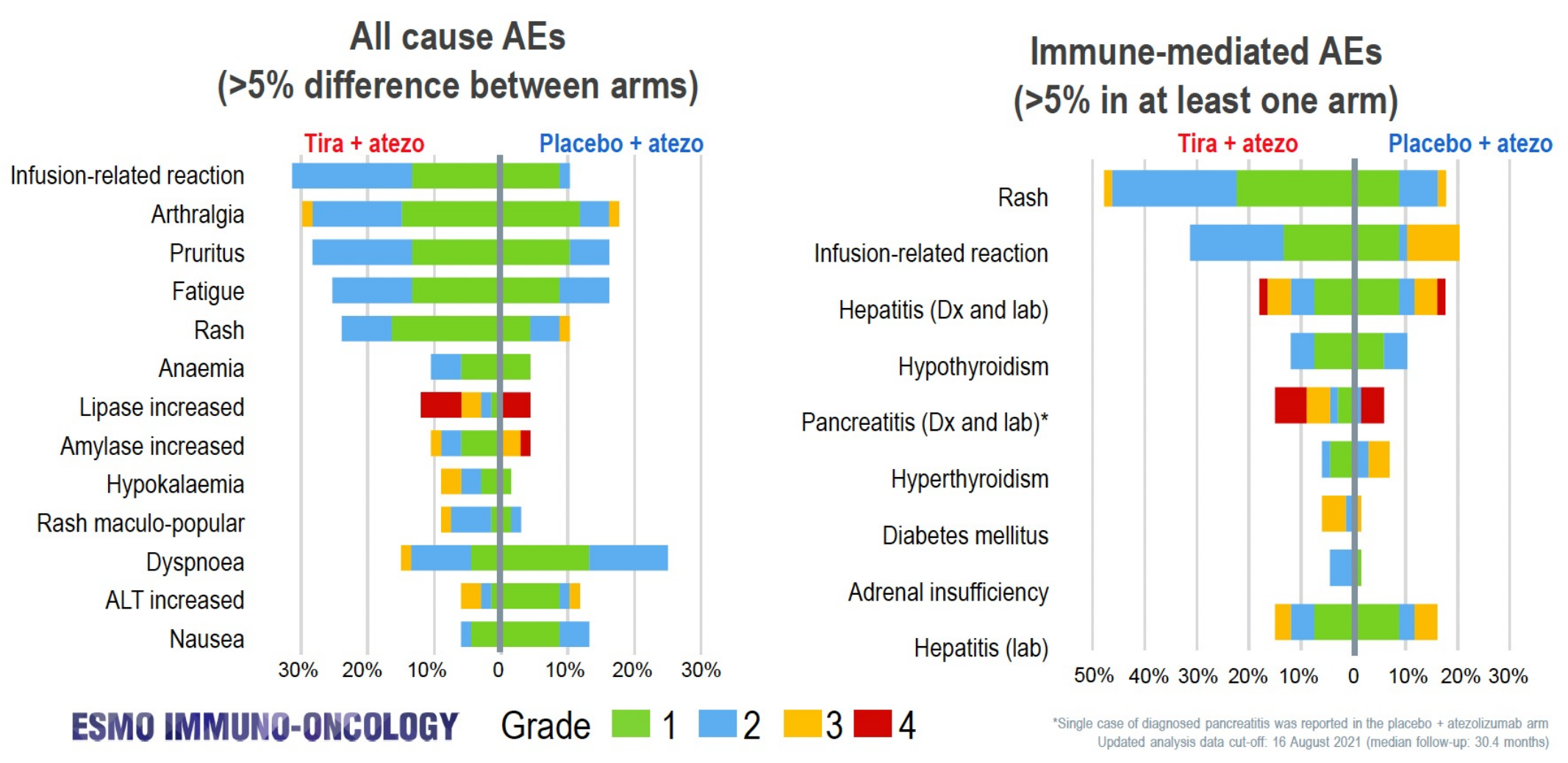
Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Safety Summary

	Tiragolumab + atezolizumab (n=67)	Placebo + atezolizumab (n=68)
Median treatment duration, months (min–max)	4.99 (0–34.5)	2.81 (0–30.3)
Any-cause AEs, n (%)	66 (98.5)	66 (97.1)
Grade 3–4 AEs	35 (52.2)	27 (39.7)
Grade 5	3 (4.5)	7 (10.3)
Serious AEs	35 (52.2)	28 (41.2)
Treatment-related AEs, n (%)	55 (82.1)	48 (70.6)
Grade 3–4 AEs	15 (22.4)	17 (25.0)
Grade 5*	2 (3.0)	0
Serious AEs	14 (20.9)	12 (17.6)
Immune-mediated AEs, n (%)	51 (76.1)	32 (47.1)
Grade 3–4	13 (19.4)	11 (16.2)
AEs leading to dose modification/interruption, n (%)	33 (49.3)	24 (35.3)
AEs leading to treatment withdrawal, n (%)	10 (14.9)	9 (13.2)

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Incidence of Adverse Events

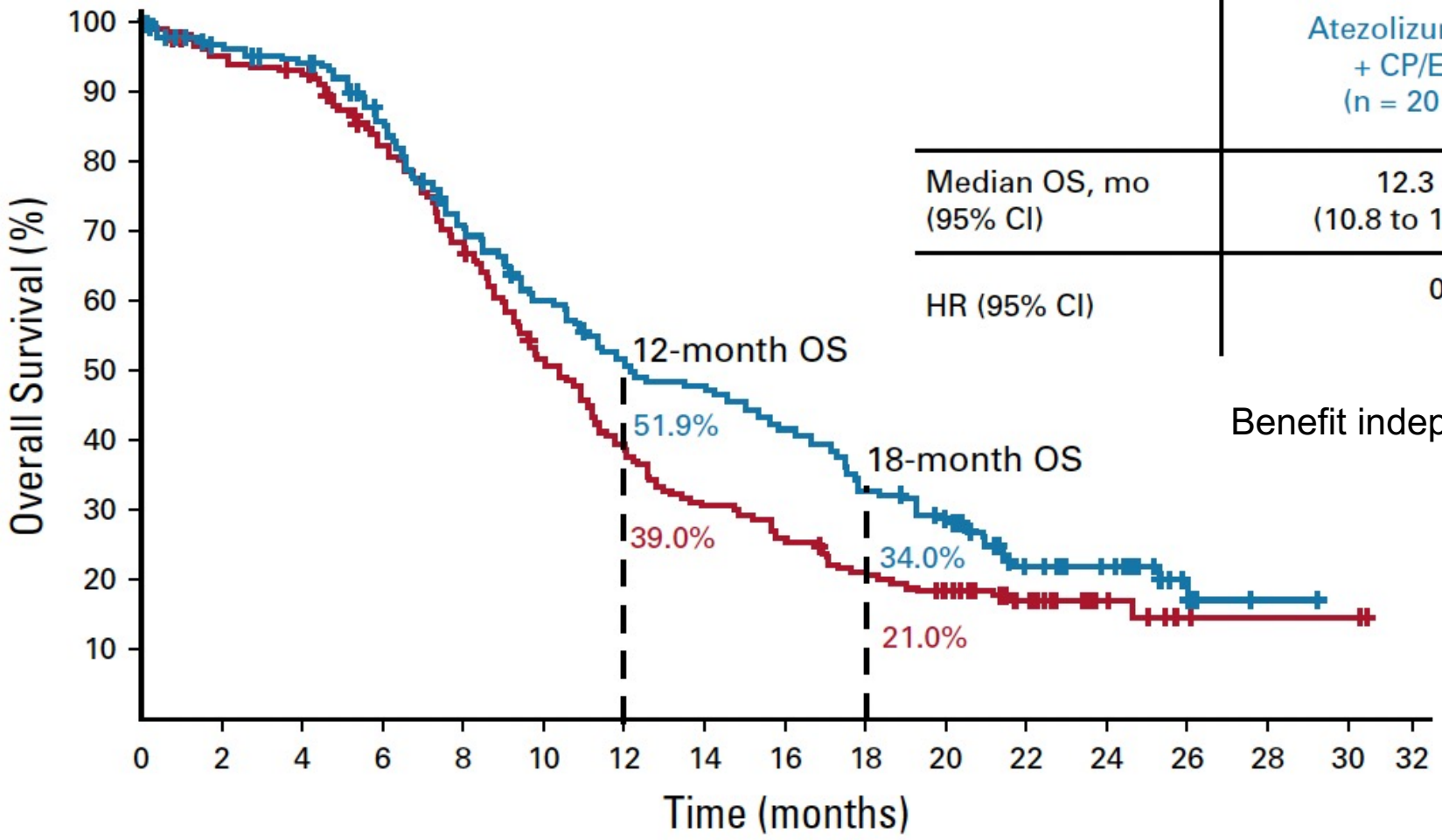


Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

Role of Immunotherapy for Small Cell Lung Cancer (SCLC)

IMpower133: Updated OS in Extensive-Stage SCLC (ES-SCLC) Treated with First-Line Atezolizumab, Carboplatin and Etoposide

Median follow up: 22.9 mo



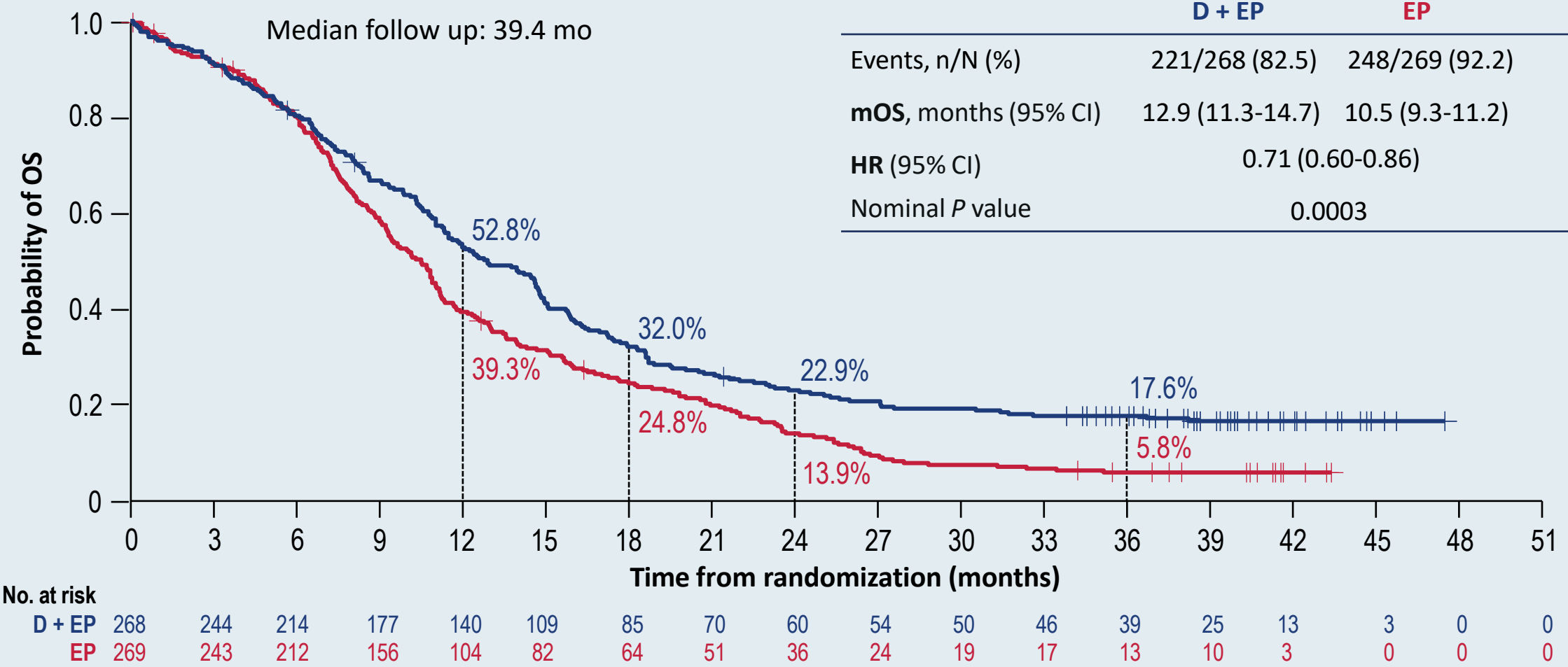
	Atezolizumab + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8 to 15.8)	10.3 (9.3 to 11.3)
HR (95% CI)	0.76 (0.60 to 0.95) *P* = .0154*	

Benefit independent of PD-L1 status

Liu SV et al. *J Clin Oncol* 2021;39(6):619-30.

RTP RESEARCH TO PRACTICE

CASPIAN: Three-Year Updated OS with First-Line Durvalumab, Platinum and Etoposide for ES-SCLC



	D + EP	EP
Events, n/N (%)	221/268 (82.5)	248/269 (92.2)
mOS, months (95% CI)	12.9 (11.3-14.7)	10.5 (9.3-11.2)
HR (95% CI)	0.71 (0.60-0.86)	
Nominal *P* value	0.0003	

Paz-Ares LG et al. ESMO 2021;Abstract LBA61.

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Dose-Schedule for Maintenance Atezolizumab versus Durvalumab: Does it Matter to Patients?

Durvalumab Prescribing Information

- Weight 30 kg and more: With etoposide and either carboplatin or cisplatin, administer durvalumab 1500 mg every 3 weeks in combination with chemotherapy, and then *1500 mg every 4 weeks as a single agent*
- Weight less than 30 kg: With etoposide and either carboplatin or cisplatin, administer durvalumab 20 mg/kg every 3 weeks in combination with chemotherapy, and then *10 mg/kg every 2 weeks as a single agent*

Atezolizumab Prescribing information

- Administer atezolizumab as 840 mg every 2 weeks, 1200 mg every 3 weeks, or *1680 mg every 4 weeks*

Durvalumab Prescribing information (rev 7/2021); Atezolizumab prescribing information (rev 1/2022);

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Thursday, February 24, 2022
5:00 PM – 6:00 PM ET

Faculty
Amir Fathi, MD

Moderator
Neil Love, MD

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Thank you for joining us!

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

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