Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Non-Small Cell Lung Cancer

Thursday, July 8, 2021
5:00 PM – 6:00 PM ET

Faculty

Zofia Piotrowska, MD, MHS
Tara Plues, APRN, MSN

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Zofia Piotrowska, MD, MHS
Assistant Professor of Medicine
Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts

Tara Plues, APRN, MSN
Hematology and Medical Oncology
Cleveland Clinic
Cleveland, Ohio

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Merck, Regeneron Pharmaceuticals Inc and Sanofi Genzyme, and Takeda Oncology.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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Dr Piotrowska — Disclosures

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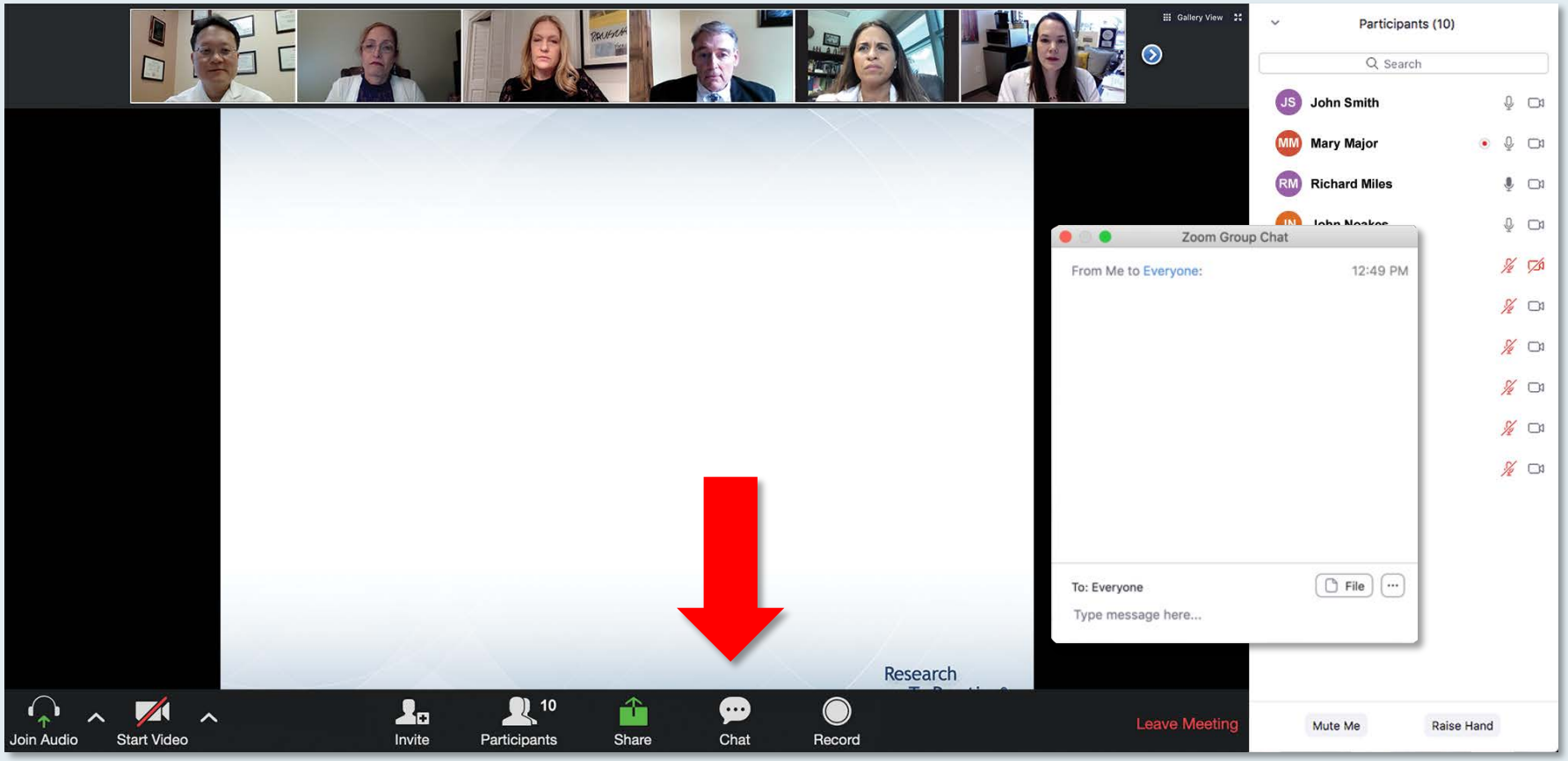
Ms Plues — Disclosures

No relevant conflicts of interest to disclose

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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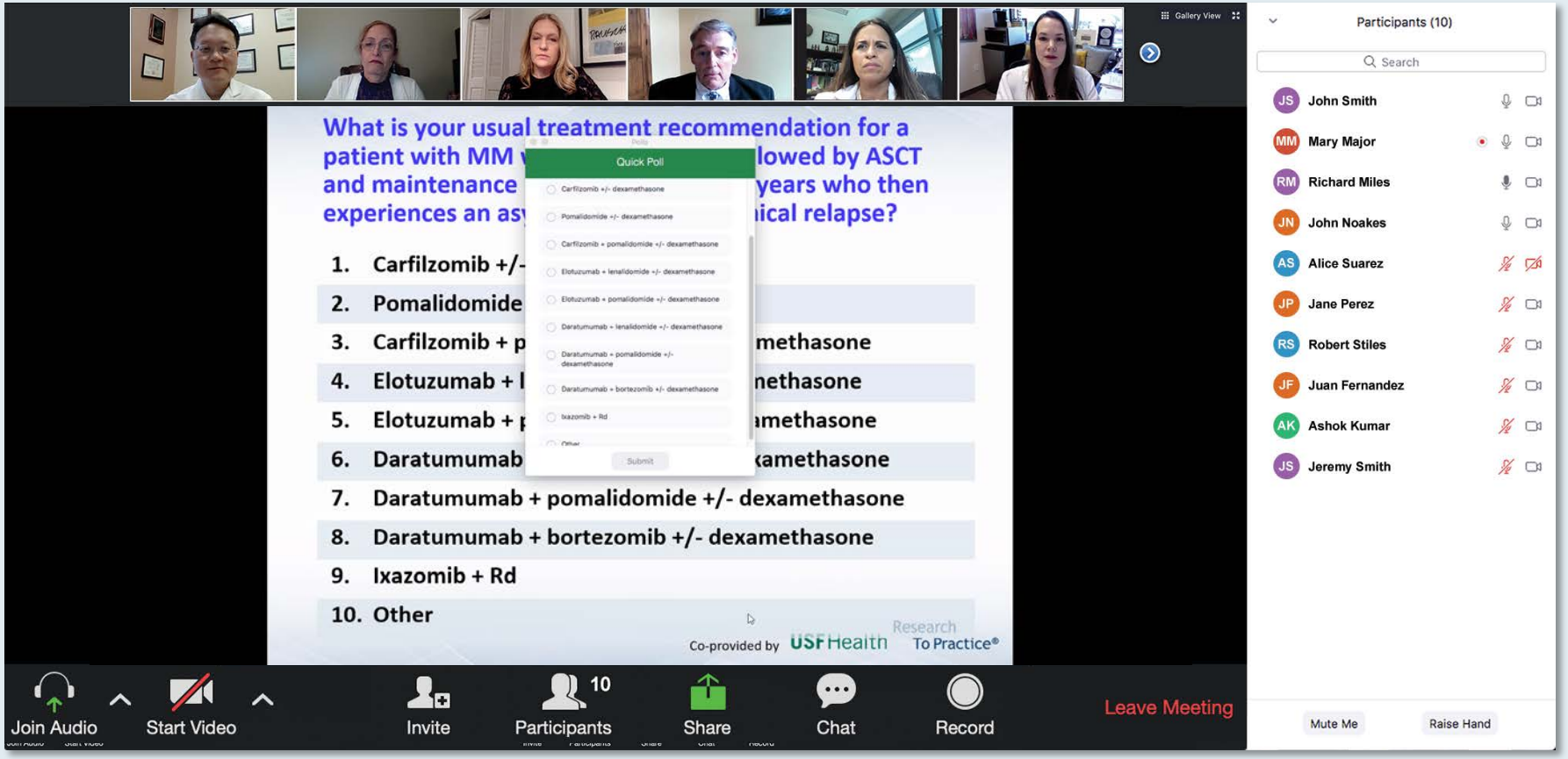
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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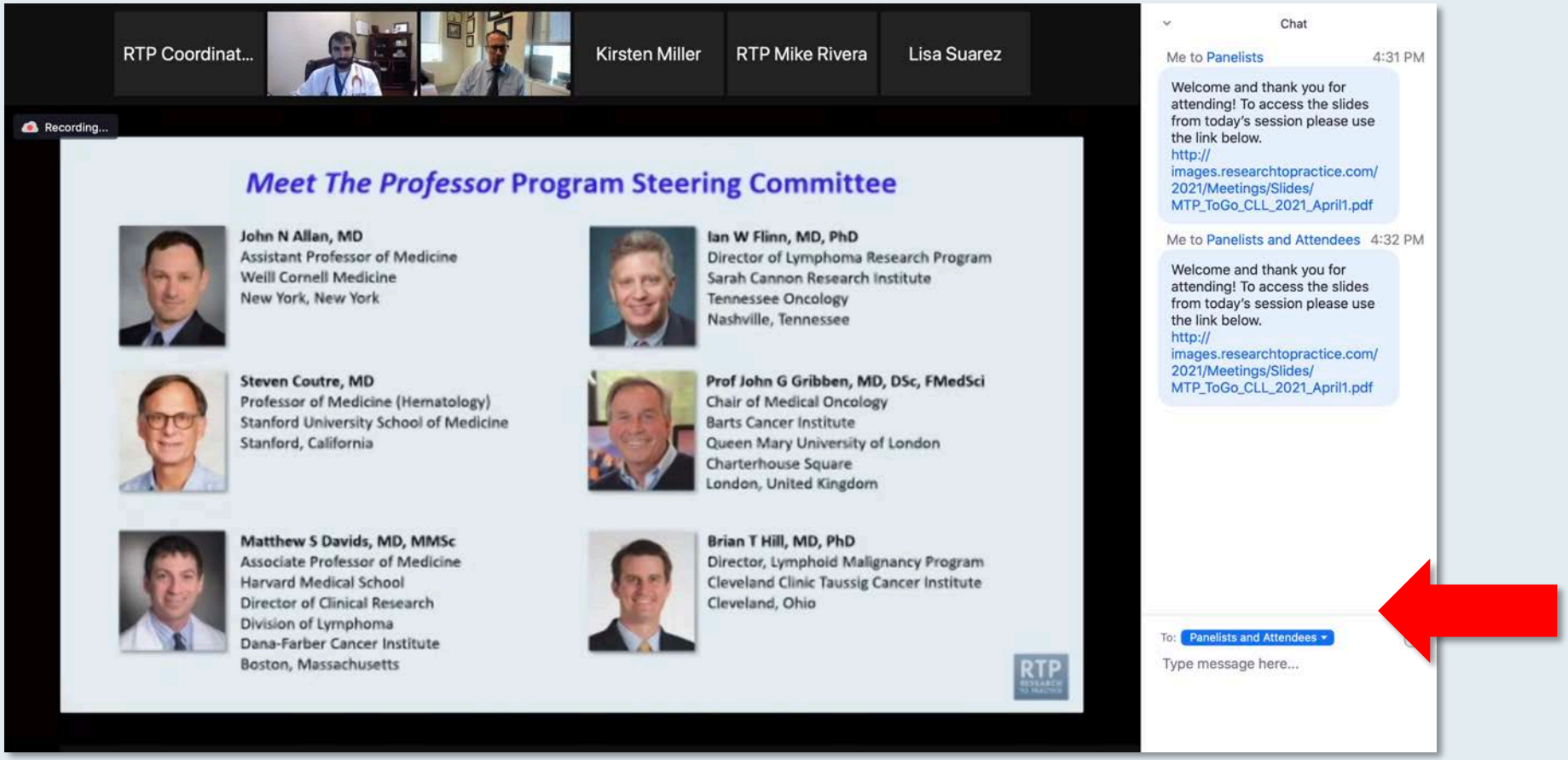
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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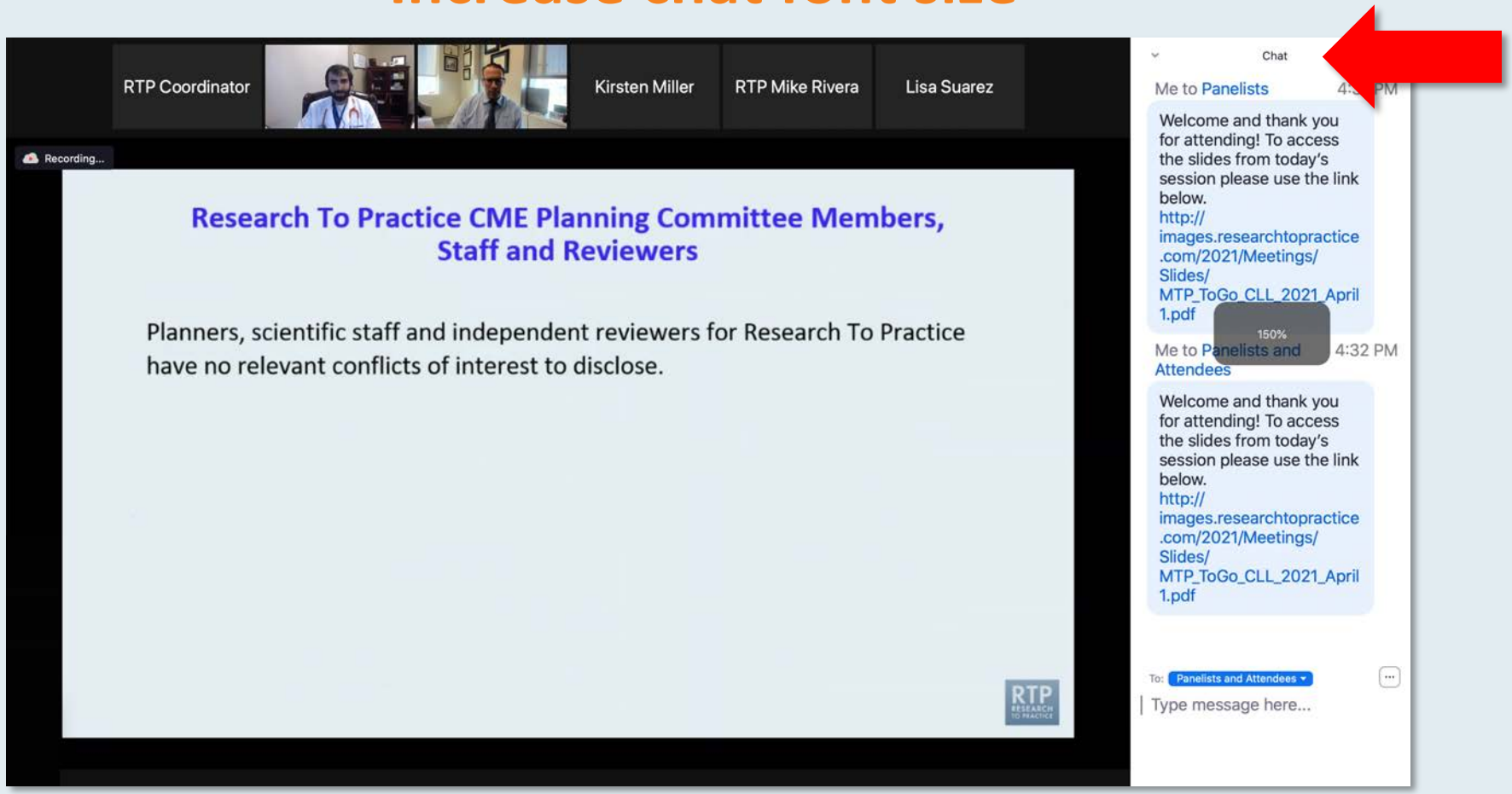
Increase chat font size



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

Management of Localized Non-Small Cell Lung Cancer with EGFR Tumor Mutations

DR ROY HERBST

YALE CANCER CENTER

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A Conversation with the Investigators: Hormonal Therapy for Prostate Cancer

Monday, July 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Simon Chowdhury, MD, PhD
Tanya B Dorff, MD
Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Chimeric Antigen Receptor T-Cell Therapy in Hematologic Cancers

Tuesday, July 13, 2021
5:00 PM – 6:00 PM ET

Faculty

Caron Jacobson, MD
David G Maloney, MD, PhD
Nikhil C Munshi, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Acute Myeloid Leukemia and Myelodysplastic Syndromes

Wednesday, July 14, 2021
5:00 PM – 6:00 PM ET

Faculty

Courtney D DiNardo, MD, MSCE
Gail J Roboz, MD
Eytan M Stein, MD

Moderator

Neil Love, MD

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Gynecologic Cancers

Thursday, July 15, 2021
5:00 PM – 6:00 PM ET

Faculty

Krishnansu S Tewari, MD
Courtney Arn, CNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Metastatic Castration-Resistant Prostate Cancer

Tuesday, July 20, 2021
5:00 PM – 6:00 PM ET

Faculty

Emmanuel S Antonarakis, MD
Johann de Bono, MBChB, MSc, PhD
Julie N Graff, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Bladder Cancer

Wednesday, July 21, 2021
5:00 PM – 6:00 PM ET

Faculty

Petros Grivas, MD, PhD
Daniel P Petrylak, MD
Arlene Siefker-Radtke, MD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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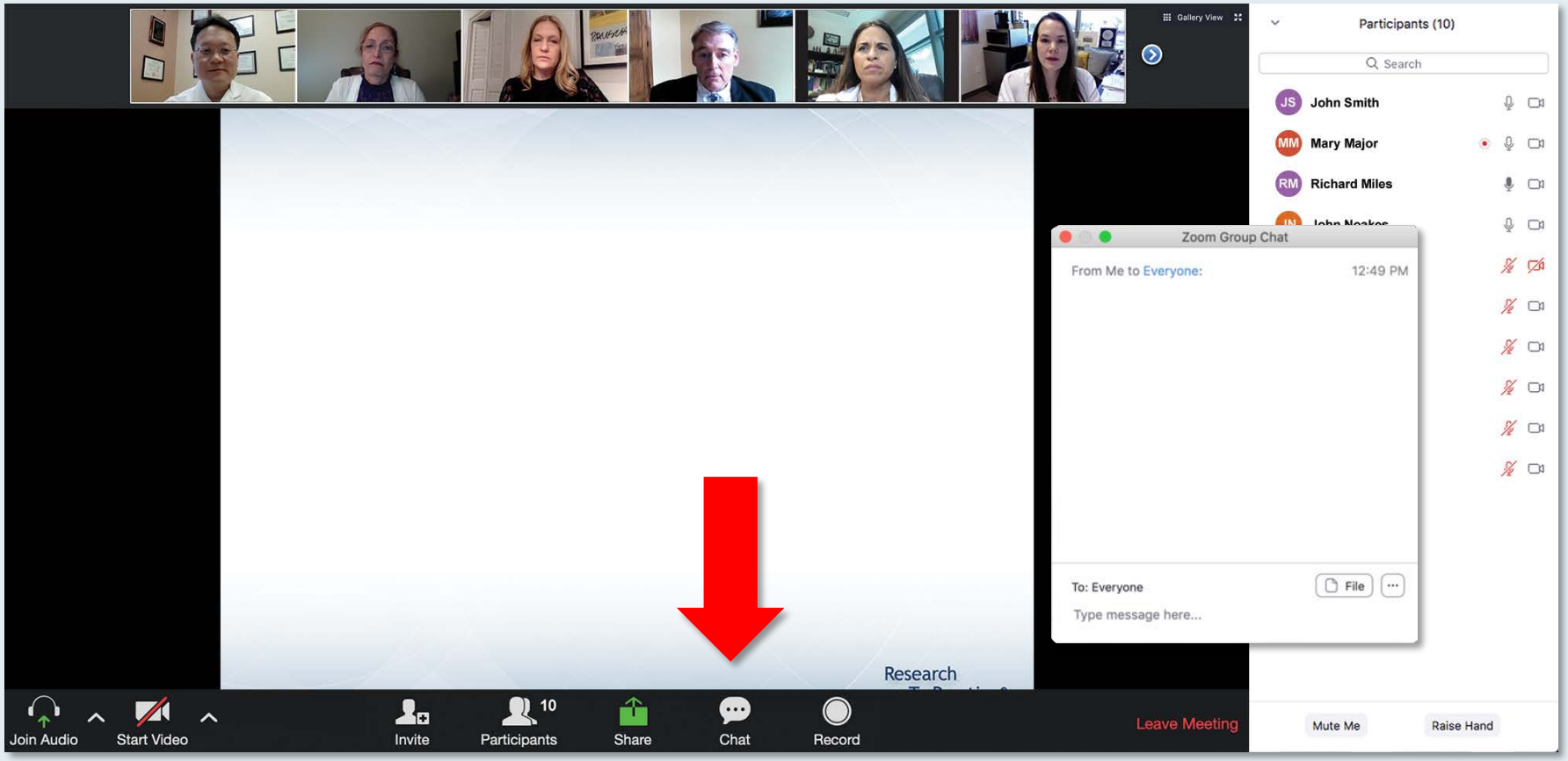

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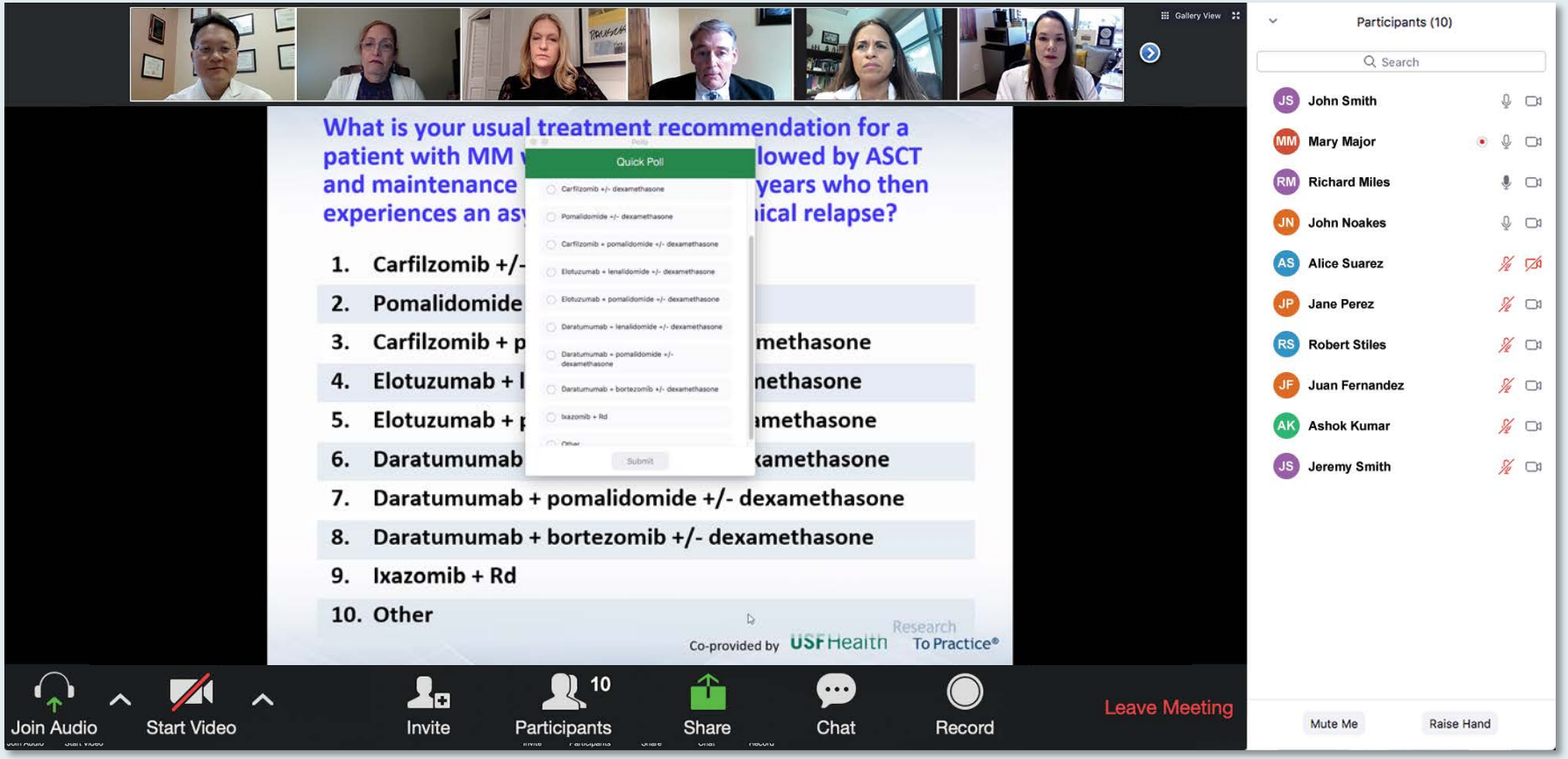

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RTP RESEARCH TO PRACTICE

Oncology Grand Rounds Nursing Webinar Series

April 2021

Monday	Tuesday	Wednesday	Thursday	Friday
19	20 Breast Ca 8:30 AM Lung Ca 5:00 PM	21 AML 12:00 PM CRC and GE Ca 4:45 PM	22 Prostate Ca 8:30 AM Lymphomas 5:00 PM	23
26	27 Multiple Myeloma 8:30 AM GYN 5:00 PM	28 Bladder Ca 12:00 PM	29 CLL 8:30 AM CAR-T 5:00 PM	30

RTP RESEARCH TO PRACTICE

13th Annual Oncology Grand Rounds

A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress

Non-Small Cell Lung Cancer

Tuesday, April 20, 2021
5:00 PM – 6:30 PM ET

Medical Oncologists

John V Heymach, MD, PhD
Paul K Paik, MD
Zofia Piotrowska, MD, MHS

Oncology Nurse Practitioners

Kelly EH Goodwin, MSN, RN, ANP-BC
Tara Plues, APRN, MSN
Victoria Sherry, DNP, CRNP, AOCNP

Moderator

Neil Love, MD

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Tara Plues, APRN, MSN


Kelly EH Goodwin, MSN, RN, ANP-BC


Victoria Sherry, DNP, CRNP, AOCNP

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Agenda

- Case 1: A 52-year-old woman with NSCLC with an EGFR exon 19 mutation
  - Key Recent Data Sets – ADAURA, FLAURA, BLOOM trials
- Case 2: A 64-year-old man with newly diagnosed metastatic adenocarcinoma of the lung – PD-L1 95%
  - Key Recent Data Sets – KEYNOTE-001 trial, Study 1624
- Case 3: A 64-year-old woman with metastatic NSCLC with a HER2 mutation and PD-L1 40%
  - Key Recent Data Sets – PACIFIC, DESTINY-Lung01 trials
- Case 4: A 60-year-old man with newly diagnosed metastatic NSCLC with an ALK rearrangement
- Case 5: A 46-year-old woman with metastatic NSCLC with an EGFR exon 20 tumor mutation
  - Key Recent Data Sets – EXCLAIM, CHRYSALIS trials

Agenda

- **Case 1: A 52-year-old woman with NSCLC with an EGFR exon 19 mutation**
  - **Key Recent Data Sets – ADAURA, FLAURA, BLOOM trials**
- **Case 2: A 64-year-old man with newly diagnosed metastatic adenocarcinoma of the lung – PD-L1 95%**
  - **Key Recent Data Sets – KEYNOTE-001 trial, Study 1624**
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- **Case 4: A 60-year-old man with newly diagnosed metastatic NSCLC with an ALK rearrangement**
- **Case 5: A 46-year-old woman with metastatic NSCLC with an EGFR exon 20 tumor mutation**
  - **Key Recent Data Sets – EXCLAIM, CHRYSALIS trials**

Case Presentation – A 52-year-old woman with NSCLC with an EGFR exon 19 mutation

- Diagnosed with Stage IIA NSCLC
- Right lobectomy → adjuvant cisplatin/pemetrexed x 4
- In-house pathology review reveals exon 19 mutation
- Adjuvant osimertinib
    - Mild dry skin on hands, otherwise tolerating treatment well

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Targetable tumor driver mutations in non-small cell lung cancer (NSCLC) generally occur in patients with…

1. Nonsquamous cancer
2. Squamous cancer
3. Both a and b
4. Neither a nor b
5. I don’t know

Compared to erlotinib, osimertinib…

1. Causes less skin toxicity
2. Has greater antitumor efficacy
3. Has a greater antitumor effect in the CNS
4. All of the above
5. Only a and b
6. Only b and c
7. Only a and c
8. I don’t know

Targetable Oncogenic Drivers – Approved or Investigational Agents

EGFR exon 20
- Amivantamab
- Mobocertinib
- Poziotinib

EGFR sensitizing
- Gefitinib
- Erlotinib
- Afatinib
- Osimertinib
- Dacomitinib
- Necitumumab
- Rociletinib

ALK
- Crizotinib
- Alectinib
- Ceritinib
- Lorlatinib
- Brigatinib

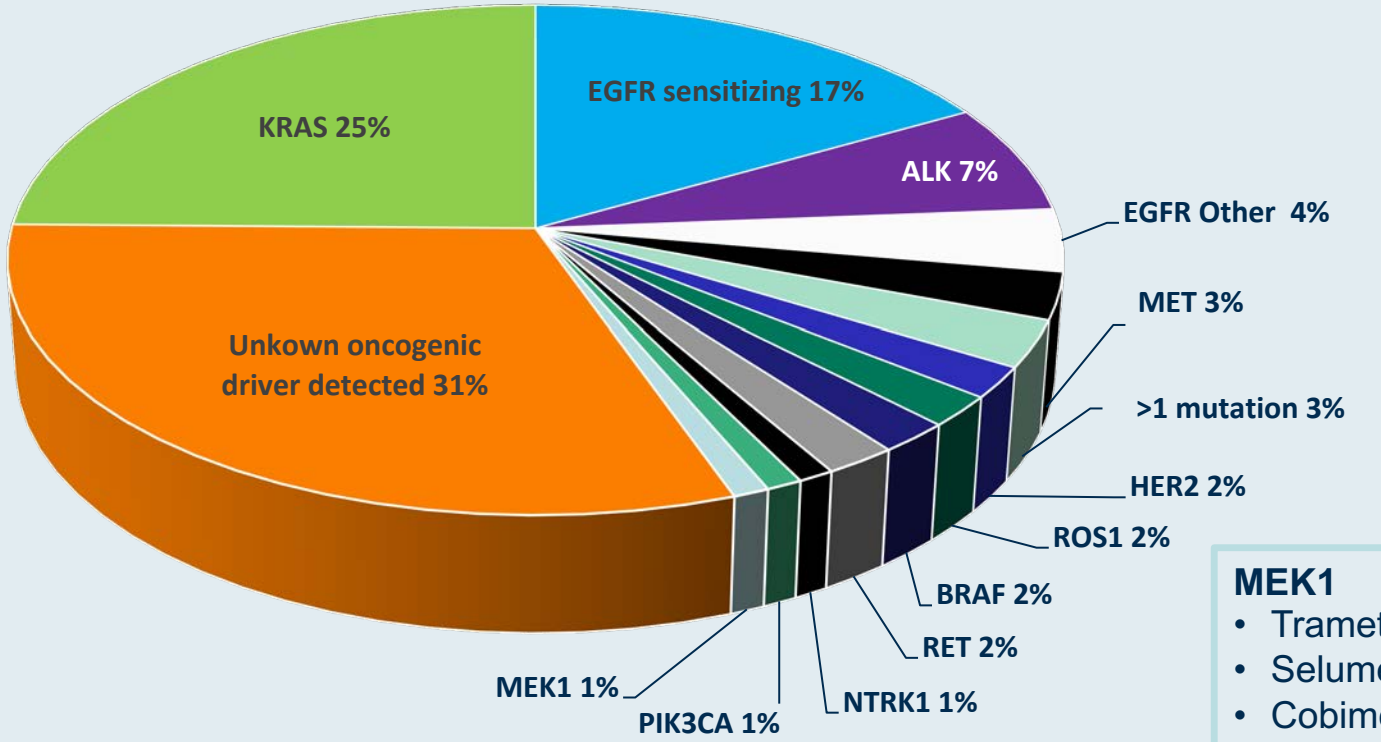
MET
- Crizotinib
- Cabozantinib

MET exon 14
- Capmatinib
- Tepotinib

HER2
- Trastuzumab deruxtecan
- Trastuzumab emtansine
- Afatinib
- Dacomitinib

ROS1
- Crizotinib
- Cabozantinib
- Ceritinib
- Lorlatinib
- Entrectinib

BRAF
- Vemurafenib
- Dabrafenib
- Encorafenib



RET
- Cabozantinib
- Alectinib
- Apatinib
- Vandetanib
- Ponatinib
- Lenvatinib
- Pralsetinib
- Selpercatinib

MEK1
- Trametinib
- Selumetinib
- Cobimetinib

KRAS G12C
- Sotorasib

NTRK1
- Entrectinib
- Larotrectinib
- Cabozantinib
- Taletrectinib

Modified from Frances Shepherd ASCO Annual Meeting 2019.

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FDA Approves Osimertinib as Adjuvant Therapy for NSCLC with EGFR Mutations

Press Release – December 18, 2020

"The Food and Drug Administration approved osimertinib for adjuvant therapy after tumor resection in patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.

Efficacy was demonstrated in a randomized, double-blind, placebo-controlled trial (ADAURA, NCT02511106) in patients with EGFR exon 19 deletions or exon 21 L858R mutation-positive NSCLC who had complete tumor resection, with or without prior adjuvant chemotherapy. Eligible patients with resectable tumors (stage IB – IIIA) were required to have predominantly non-squamous histology and EGFR exon 19 deletions or exon 21 L858R mutations identified prospectively from tumor tissue in a central laboratory by the cobas® EGFR Mutation Test. A total of 682 patients were randomized (1:1) to receive osimertinib 80 mg orally once daily or placebo following recovery from surgery and standard adjuvant chemotherapy, if given.

www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-osimertinib-adjuvant-therapy-non-small-cell-lung-cancer-egfr-mutations

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

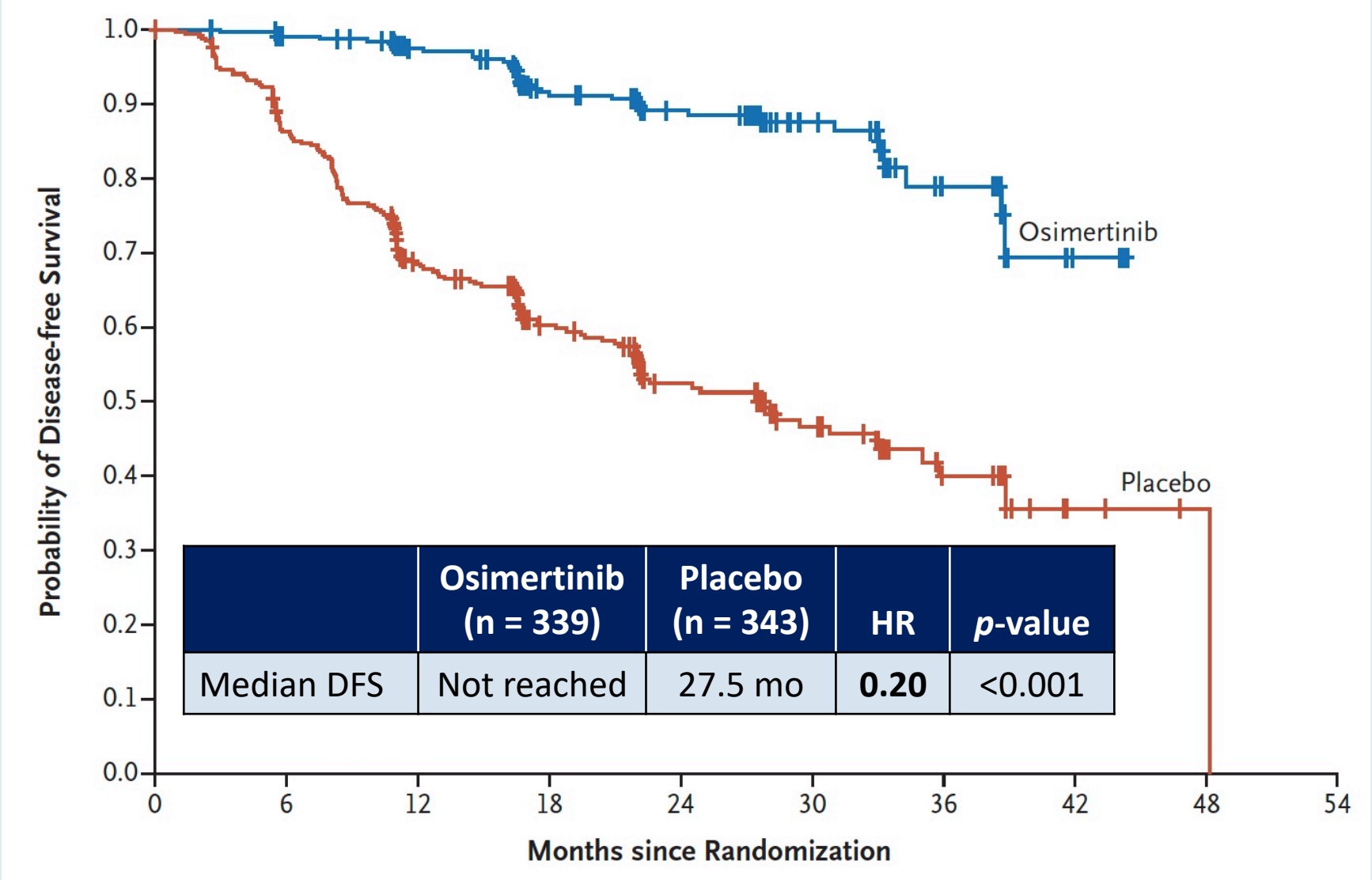
The NEW ENGLAND JOURNAL of MEDICINE

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., for the ADAURA Investigators*

ADAURA: Disease-Free Survival in Stage IB to IIIA Disease



	Osimertinib (n = 339)	Placebo (n = 343)	HR	*p*-value
Median DFS	Not reached	27.5 mo	**0.20**	<0.001

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

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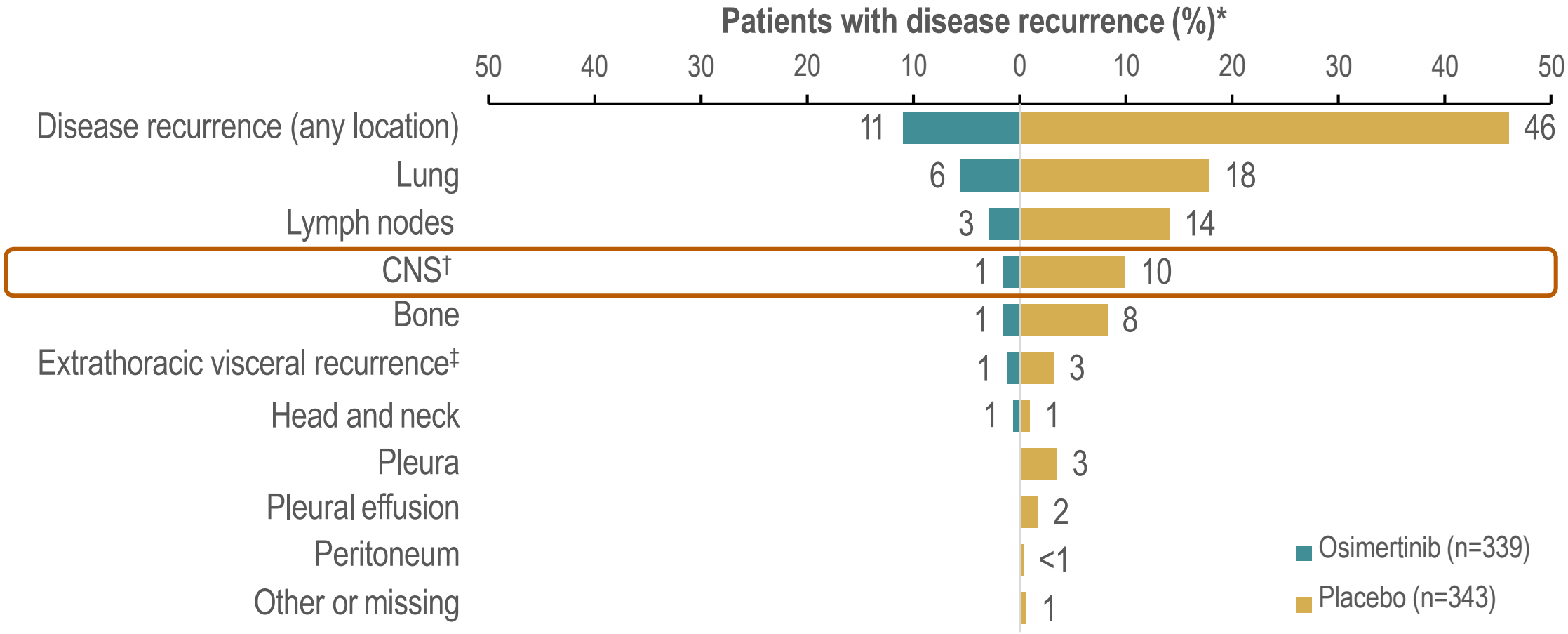
ADAURA: Sites of disease recurrence



*Number of patients with disease recurrence regardless of pathology results of the tumour recurrence location;
†Includes CNS only (osimertinib n=4 [1%]; placebo n=25 [7%]) and CNS plus other locations (osimertinib n=1 [<1%]; placebo n=9 [3%]).
One patient in the osimertinib arm and one patient in the placebo arm had CNS metastases at baseline; therefore, these two patients were censored on Day 1 and excluded from the CNS DFS efficacy analysis;
‡Includes disease recurrence in liver, renal and adrenal systems and pancreas.
ADAURA data cut-off: 17 January, 2020

Tsuboi M et al. ESMO 2020;Abstract LBA1.

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%)

*Defined as CNS disease recurrence, or death without any CNS disease recurrence;
†Death in absence of CNS disease recurrence, or death within two visits of baseline where the patient has no evaluable assessments or no baseline data.
ADAURA data cut-off: 17 January, 2020

Tsuboi M et al. ESMO 2020;Abstract LBA1.

ADAURA: Most Common Treatment-Related Adverse Events

Adverse events	Osimertinib (n = 337)	Placebo (n = 343)
Dose interruptions due to AE	24%	11%
Dose reductions due to AE	9%	1%
Discontinuation of treatment due to AE	11%	3%
Diarrhea	39%	14%
Paronychia	23%	1%
Dry skin	20%	5%
Pruritus	17%	7%
Stomatitis	16%	2%

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

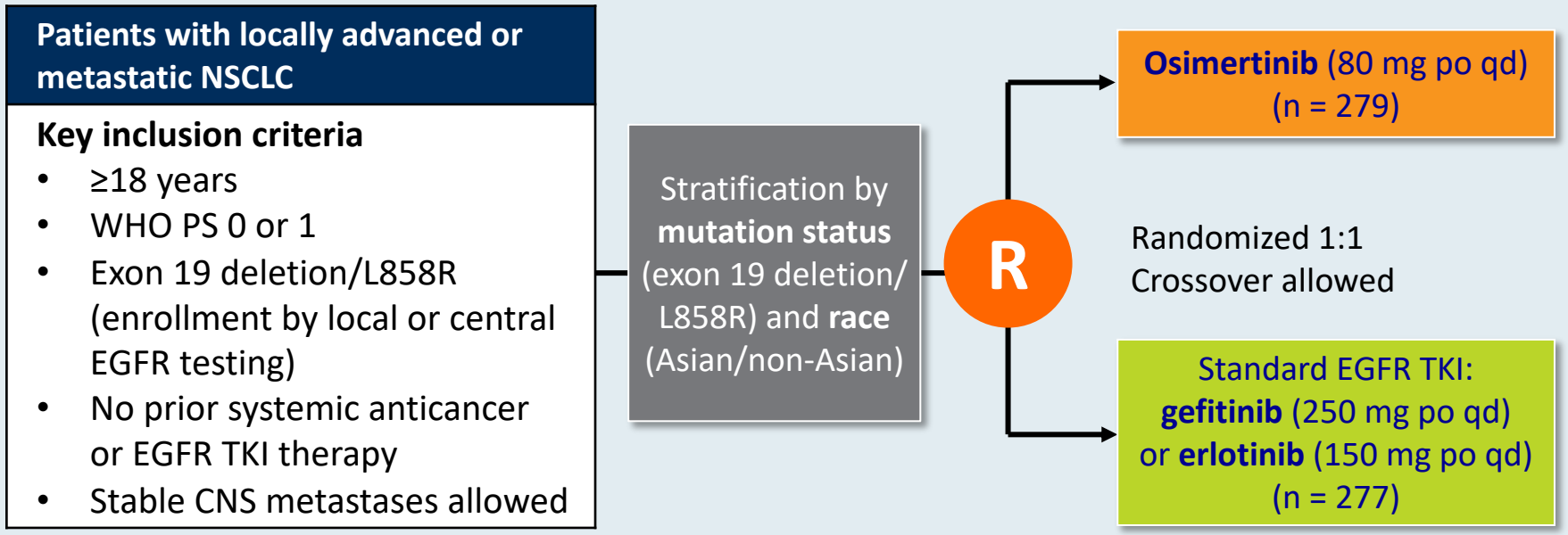
Which of the following assays are considered standard in the evaluation of newly diagnosed metastatic NSCLC?

1. Multiplex genomic testing/NGS (next-generation sequencing)
2. PD-L1 assay
3. Both a and b
4. Neither a nor b
5. I don’t know

In general, what is the most common initial treatment for patients with previously untreated NSCLC with an EGFR tumor mutation and multiple, bilateral asymptomatic brain metastases that would require whole-brain radiation therapy?

1. Whole-brain radiation therapy followed by osimertinib
2. Whole-brain radiation therapy
3. Chemotherapy
4. Osimertinib
5. Erlotinib
6. I don’t know

FLAURA: A Phase III Study of Osimertinib versus Gefitinib or Erlotinib as First-Line Treatment for Advanced NSCLC with EGFR Tumor Mutation



Primary endpoint: Progression-free survival (PFS) based on investigator assessment (per RECIST 1.1)
Key secondary endpoints: Objective response rate, overall survival and quality of life

NSCLC= non-small cell lung cancer; TKI = tyrosine kinase inhibitor

www.clinicaltrials.gov. March 2020; Soria JC et al. *N Engl J Med* 2018;378(2):113-25.

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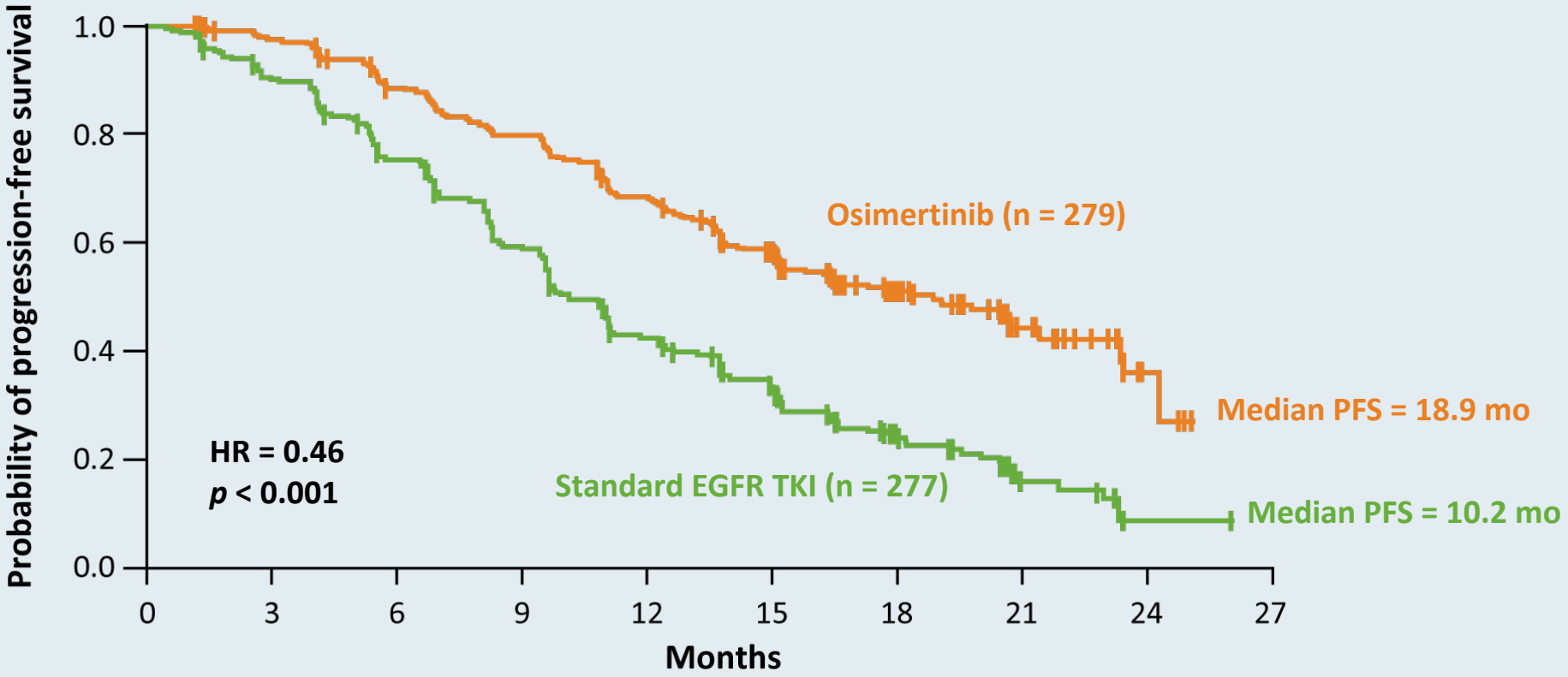
FLAURA: PFS with Osimertinib for Patients with NSCLC and EGFR Tumor Mutations

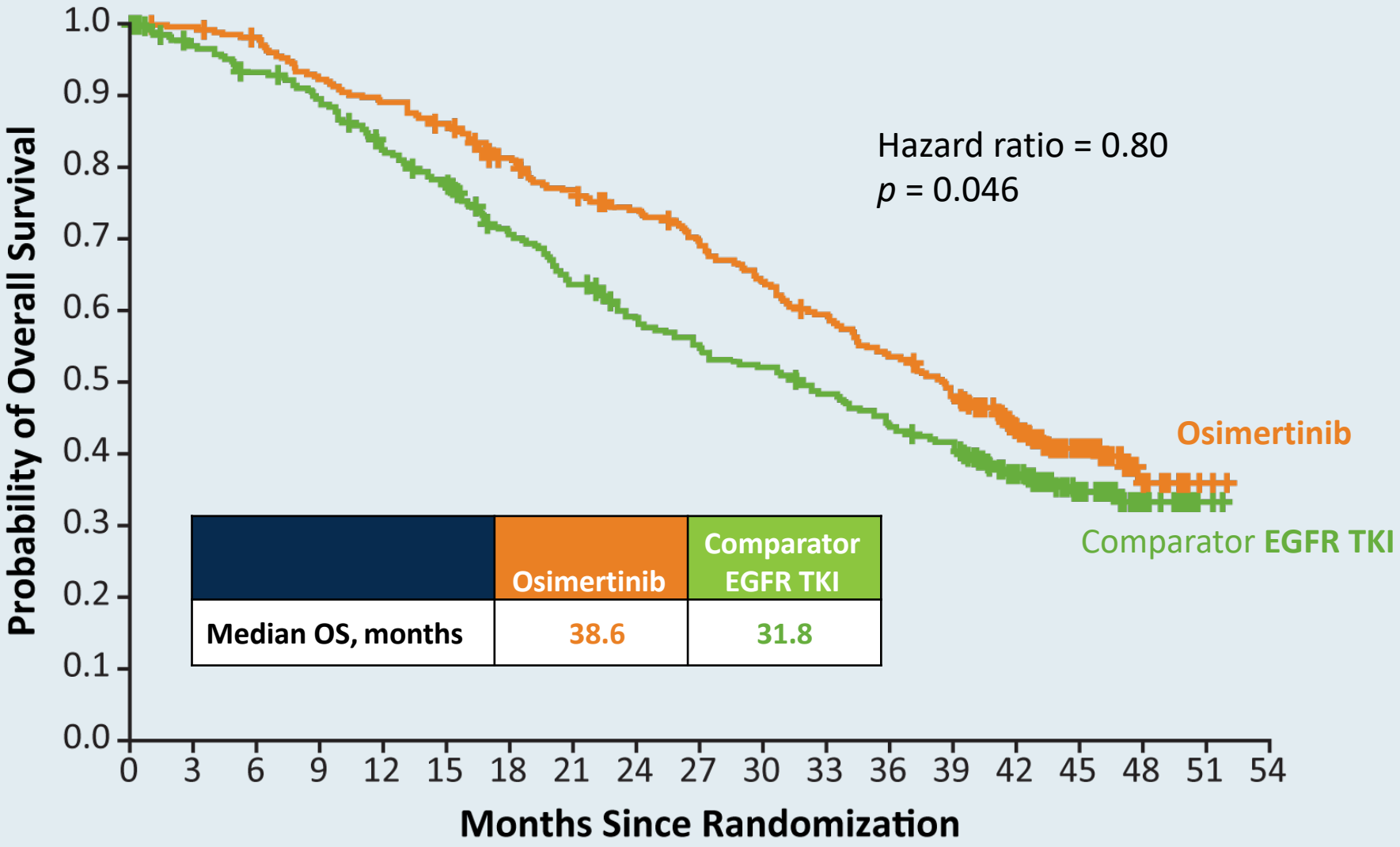
FLAURA primary endpoint: PFS for patients with EGFR exon 19 del or L858R mutation (full analysis set)[1]



Interim overall survival (data immature), HR = 0.63, $p = 0.007$[1,2]

[1] Soria JC et al. *N Engl J Med* 2018;378(2):113-25.
[2] Planchard D et al. ELCC 2018;Abstract 128O.

FLAURA: Final Overall Survival Analysis



Ramalingam SS et al. *N Engl J Med* 2020;382(1):41-50.

CNS Efficacy of Osimertinib in Patients with Advanced NSCLC and EGFR Tumor Mutations on FLAURA Trial

FLAURA	Full-analysis set		Evaluable for response	
	Osimertinib (n = 61)	EGFR TKIs (n = 67)	Osimertinib (n = 22)	EGFR TKIs (n = 19)
CNS ORR	66%	43%	91%	68%
Median CNS DoR	Not reached	14.4 mo	15.2 mo	18.7 mo

CNS full-analysis set: measurable and nonmeasurable baseline CNS lesions; CNS evaluable for response: ≥1 measurable CNS lesion

Reungwetwattana T et al. *J Clin Oncol* 2018;[Online ahead of print].

rapid communications

Osimertinib in Patients With Epidermal Growth Factor Receptor Mutation–Positive Non–Small-Cell Lung Cancer and Leptomeningeal Metastases: The BLOOM Study

James C.H. Yang, MD, PhD[1]; Sang-We Kim, MD, PhD[2]; Dong-Wan Kim, MD, PhD[3]; Jong-Seok Lee, MD, PhD[4]; Byoung Chul Cho, MD, PhD[5]; Jin-Seok Ahn, MD, PhD[6]; Dae H. Lee, MD, PhD[2]; Tae Min Kim, MD[3]; Jonathan W. Goldman, MD[7]; Ronald B. Natale, MD[8]; Andrew P. Brown, MSc, MPhil[9]; Barbara Collins, PhD[9]; Juliann Chmielecki, PhD[10]; Karthick Vishwanathan, PhD[1,10]; Ariadna Mendoza-Naranjo, PhD[9]; and Myung-Ju Ahn, MD, PhD[6]

J Clin Oncol 2020;38(6):538-47.

BLOOM: Osimertinib in Patients with NSCLC with an EGFR Mutation and Leptomeningeal Metastases (LM)

Patients with cytologically confirmed LM received osimertinib 160 mg once daily.

	Leptomeningeal metastases (N = 37)
ORR by BICR	62%
Complete response	32%
Partial response	30%
Stable disease ≥ 6 weeks	32%
Progression	3%
Not evaluable	3%
Median DoR	15.2 months

Yang JCH et al. *J Clin Oncol* 2020;38(6):538-47.

Agenda

- Case 1: A 52-year-old woman with NSCLC with an EGFR exon 19 mutation
  - Key Recent Data Sets – ADAURA, FLAURA, BLOOM trials
- Case 2: A 64-year-old man with newly diagnosed metastatic adenocarcinoma of the lung – PD-L1 95%
  - Key Recent Data Sets – KEYNOTE-001 trial, Study 1624
- Case 3: A 64-year-old woman with metastatic NSCLC with a HER2 mutation and PD-L1 40%
  - Key Recent Data Sets – PACIFIC, DESTINY-Lung01 trials
- Case 4: A 60-year-old man with newly diagnosed metastatic NSCLC with an ALK rearrangement
- Case 5: A 46-year-old woman with metastatic NSCLC with an EGFR exon 20 tumor mutation
  - Key Recent Data Sets – EXCLAIM, CHRYSALIS trials

Case Presentation – A 64-year-old man with newly diagnosed metastatic adenocarcinoma of the lung – PD-L1 95% (Part 1)

- Diagnosed with metastatic adenocarcinoma of the lung
  - PD-L1: 95%
- Diagnosed around the same time with seropositive rheumatoid arthritis (RA)
- Pembrolizumab x 1, with significant response but exacerbation of RA requiring hospitalization
  - Held treatment x 5 months, managed by rheumatology
- Pembrolizumab re-introduced, with continued response (near NED)

Case Presentation – A 64-year-old man with newly diagnosed metastatic adenocarcinoma of the lung – PD-L1 95% (Part 2)

- Diagnosed with metastatic adenocarcinoma of the lung
  - PD-L1: 95%
- Diagnosed around the same time with seropositive RA
- Pembrolizumab x 1, with significant response but exacerbation of RA requiring hospitalization
  - Held treatment x 5 months, managed by rheumatology
- Pembrolizumab re-introduced, with continued response (near NED)
- ***Impact of the durable effects of immunotherapy***

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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TO PRACTICE

Approximately what proportion of patients with metastatic NSCLC and a PD-L1 level >50% who receive pembrolizumab will be alive in 5 years?

1. Less than 5%
2. 10%-15%
3. 20%-25%
4. 30%-40%
5. More than 50%

Checkpoint inhibitors are generally included as part of first-line treatment for patients with metastatic NSCLC and a PD-L1 level <1%.

1. Agree
2. Disagree
3. I don’t know

RTP
RESEARCH
TO PRACTICE

Cemiplimab recently received FDA approval as first-line treatment for advanced NSCLC in patients without targetable tumor mutations...

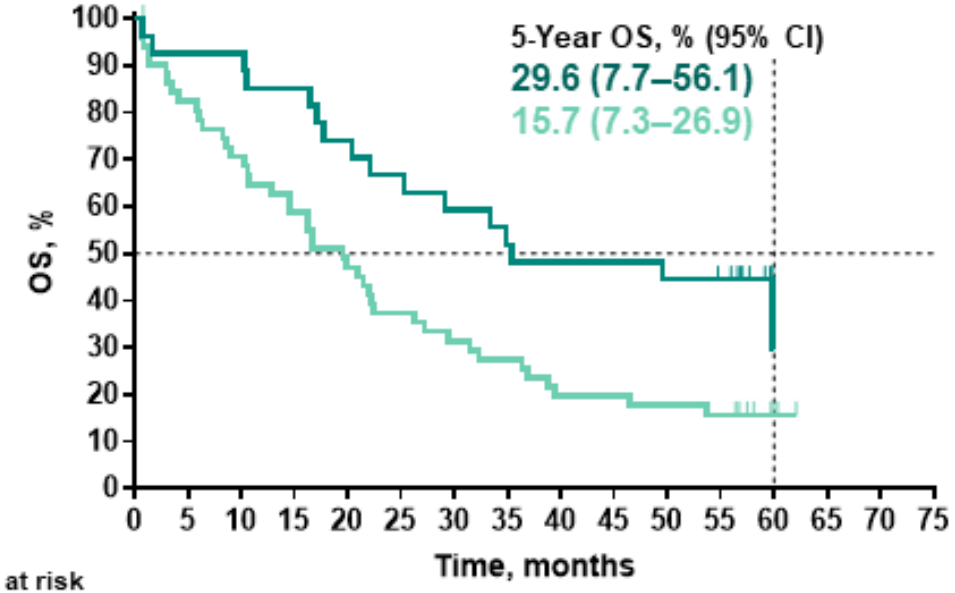
1. Regardless of PD-L1 expression
2. In tumors with high PD-L1 expression (greater than 50%)
3. I don’t know

KEYNOTE-001: Overall Survival

By PD-L1 Tumor Proportion Score (TPS)

Treatment-Naive Patients

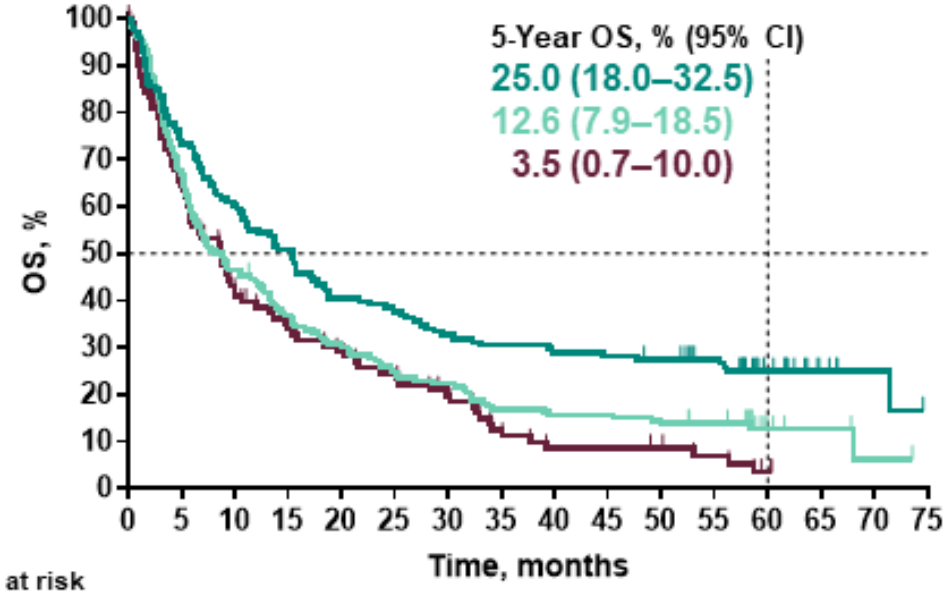
PD-L1 TPS	Events, n/N	Median (95% CI) OS, mo
TPS ≥50%	17/27	35.4 (20.3–63.5)
TPS 1%–49%	43/52	19.5 (10.7–26.3)



No. at risk																
TPS ≥50%	27	25	25	23	20	18	16	14	13	13	12	11	1	0	0	0
TPS 1%–49%	52	42	36	30	24	19	16	14	10	10	9	8	2	0	0	0

Previously Treated Patients

PD-L1 TPS	Events, n/N	Median (95% CI) OS, mo
TPS ≥50%	104/138	15.4 (10.6–18.8)
TPS 1%–49%	146/168	8.5 (6.0–12.6)
TPS <1%	83/90	8.6 (5.5–10.6)



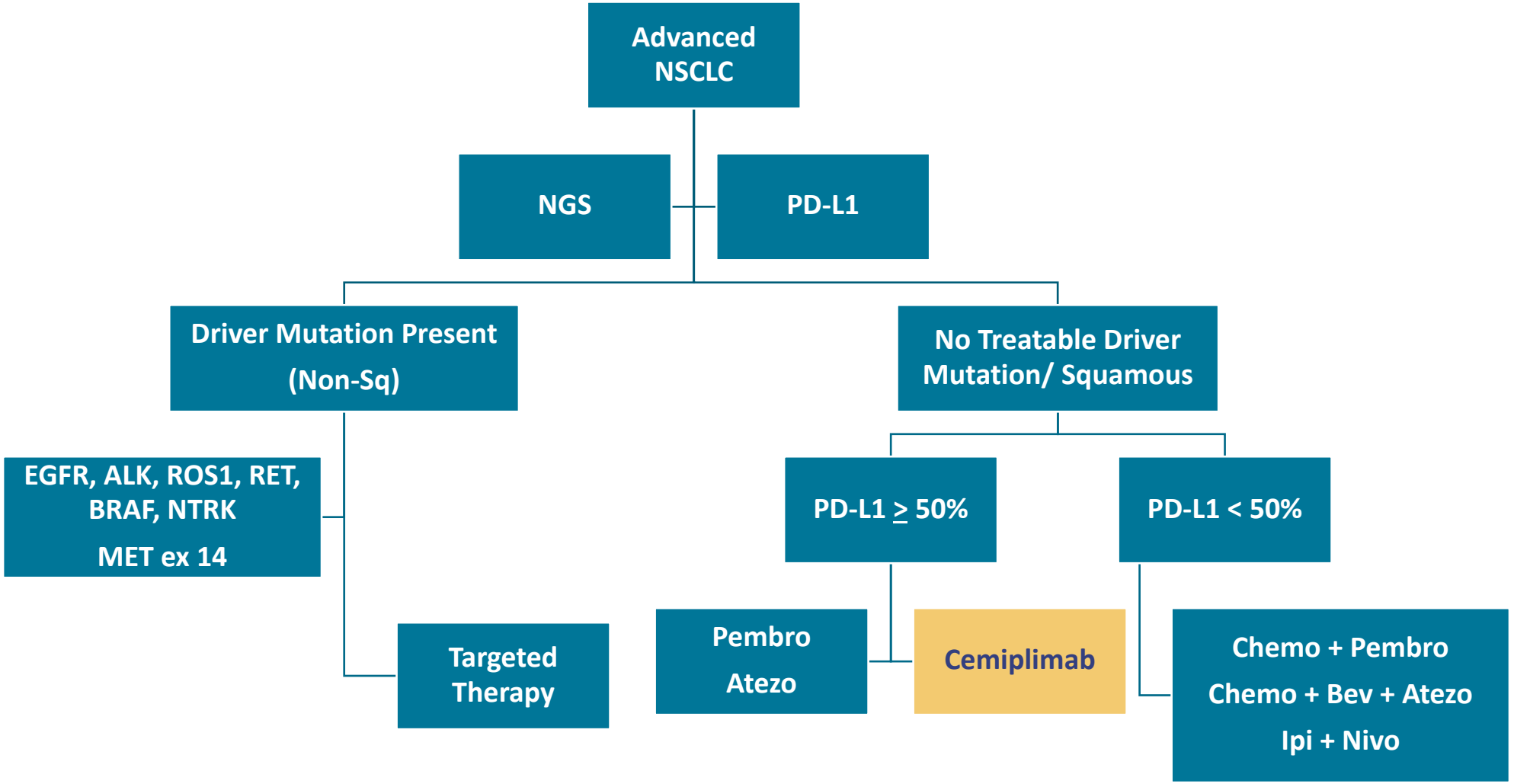
No. at risk																
TPS ≥50%	138	101	83	70	56	52	45	42	40	39	37	32	16	6	3	1
TPS 1%–49%	168	112	78	61	51	41	37	28	26	26	23	21	6	3	1	0
TPS <1%	90	58	36	29	25	21	16	10	7	7	5	4	1	0	0	0

n, number of patients who died; N, number of patients in the subgroup; OS, overall survival; PD-L1, programmed death-ligand 1; TPS, tumor proportion score.
[a]PD-L1 TPS <1% group not presented because of small patient numbers (n = 12).

Garon EB et al. ASCO 2019;Abstract LBA9015.

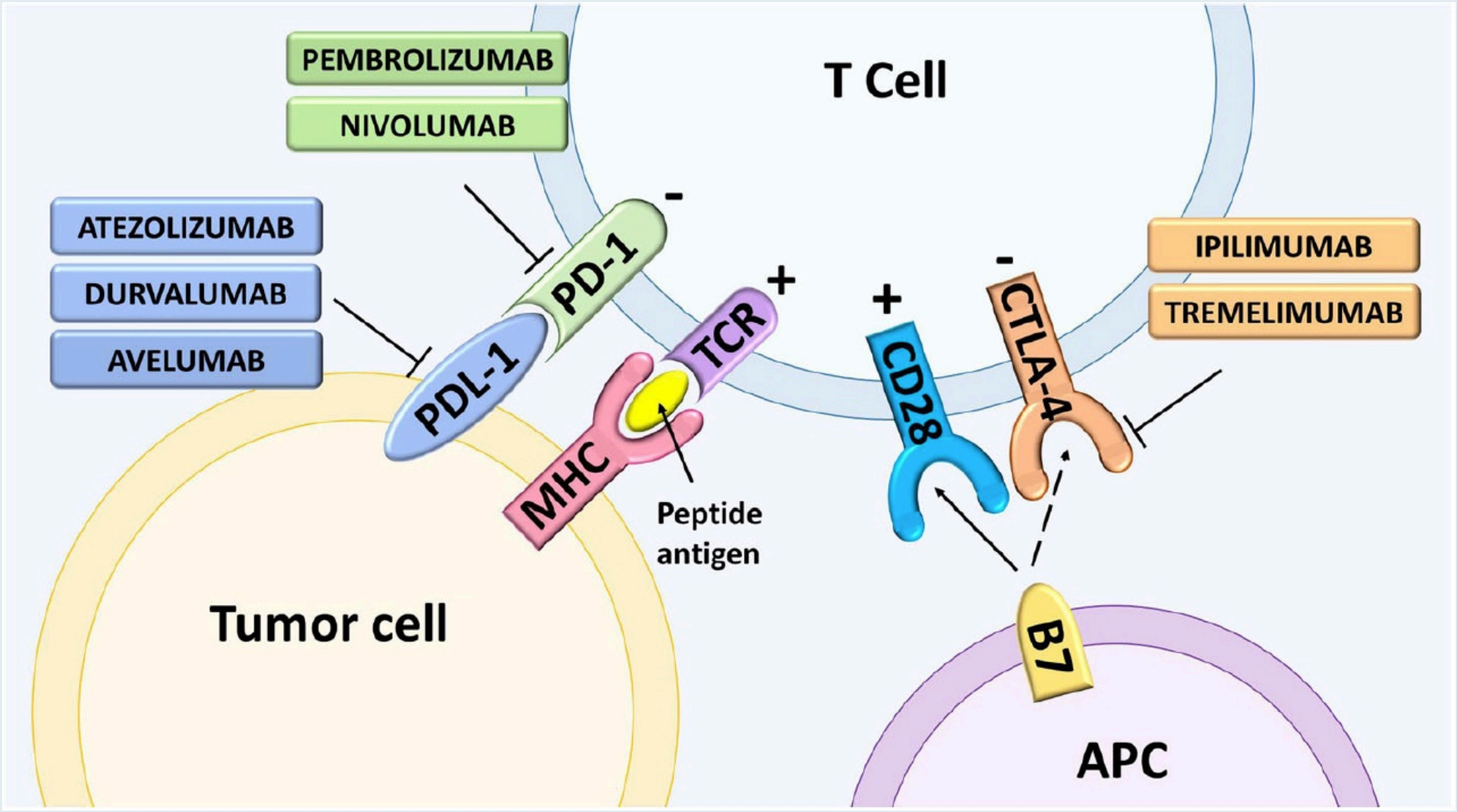
Courtesy of Edward B Garon, MD, MS

Treatment Algorithm for Advanced NSCLC



Courtesy, Suresh Ramalingam, MD

Mechanism of Action of Immune Checkpoint Inhibitors



Seebacher NA et al. JECCR 2019;38(156).

First-Line Treatment in Select Clinical Situations for Patients with Metastatic NSCLC without a Targetable Mutation

Clinical situation	Treatment questions
High PD-L1 level (>50%)	Adding chemotherapy to a checkpoint inhibitor? Nivolumab/ipilimumab?
Negative PD-L1 level (<1%)	Chemotherapy + checkpoint inhibitor? Chemotherapy + nivolumab/ipilimumab? Nivolumab/ipilimumab?

FDA-Approved Immunotherapy Combination Options for First-Line Therapy

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab + Platinum and pemetrexed[1]	8/20/18	KEYNOTE-189	Nonsquamous	0.49
Pembrolizumab + Carboplatin, paclitaxel or *nab* paclitaxel[2]	10/30/18	KEYNOTE-407	Squamous	0.64
Atezolizumab + Carboplatin and paclitaxel and bevacizumab[3]	12/6/18	IMpower150	Nonsquamous	0.78
Atezolizumab + Carboplatin and *nab* paclitaxel[4]	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab + Ipilimumab[5]	5/15/20	CheckMate-227	PD-L1 TPS ≥1, EGFR and/or ALK wt	0.62
Nivolumab + Ipilimumab and chemotherapy[6]	5/26/20	CheckMate-9LA	EGFR and/or ALK wt	0.69

[1] Gandhi. *NEJM* 2018. [2] Paz-Ares.*NEJM* 2018. [3] Socinski *NEJM* 2018. [4] West. *Lancet Oncol* 2019. [5] Hellmann. *N Engl J Med* 2019. [6] Reck. ASCO 2020;Ab 9501.

FDA-Approved Immunotherapy Monotherapy Options for First-Line Therapy (continued)

Monotherapy	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab[1,2]	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS ≥1%	0.63
Atezolizumab[3]	5/18/20	IMpower110	PD-L1 TPS ≥50, EGFR and/or ALK wt	0.59
Cemiplimab[4]	2/22/2021	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] Spigel. ESMO 2019;Ab LBA78. [4] Sezer. *Lancet* 2021.

Durvalumab and Tremelimumab with Chemotherapy Demonstrate Overall Survival Benefit in POSEIDON Trial for First-Line Stage IV NSCLC

Press Release — May 7, 2021

"Positive high-level results from the final analysis of POSEIDON showed the combination of durvalumab, tremelimumab and chemotherapy demonstrated a statistically significant and clinically meaningful overall survival (OS) benefit versus chemotherapy alone. This immunotherapy combination also demonstrated a statistically significant improvement in progression-free survival (PFS) versus chemotherapy alone, as previously reported in October 2019. Patients in this arm were treated with a short course of tremelimumab, an anti-CTLA4 antibody, over a 16-week period in addition to durvalumab and standard chemotherapy.

The durvalumab plus chemotherapy arm demonstrated a statistically significant improvement in PFS versus chemotherapy in the previous analysis, but the OS trend observed in this analysis did not achieve statistical significance. Patients in the control arm were treated with up to six cycles of chemotherapy, while those in the experimental arms were treated with up to four cycles.

Each combination demonstrated an acceptable safety profile, and no new safety signals were identified. The combination with tremelimumab delivered a broadly similar safety profile to the durvalumab and chemotherapy combination and did not lead to an increased discontinuation of treatment."

https://www.astrazeneca.com/media-centre/press-releases/2021/imfinzi-and-tremelimumab-showed-survival-in-poseidon.html

FDA Approves Cemiplimab-rwlc Monotherapy for NSCLC with High PD-L1 Expression

Press Release – February 22, 2021

"The Food and Drug Administration approved cemiplimab-rwlc for the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) (locally advanced who are not candidates for surgical resection or definitive chemoradiation or metastatic) whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] > 50%) as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations.

Efficacy was evaluated in Study 1624 (NCT03088540), a multi-center, randomized, open-label trial in 710 patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or with metastatic NSCLC. Patients were randomized (1:1) to receive cemiplimab-rwlc 350 mg intravenously every 3 weeks for up to 108 weeks or a platinum-based chemotherapy. The main efficacy outcome measures were overall survival (OS) and progression-free survival (PFS) per blinded independent central review (BICR)."

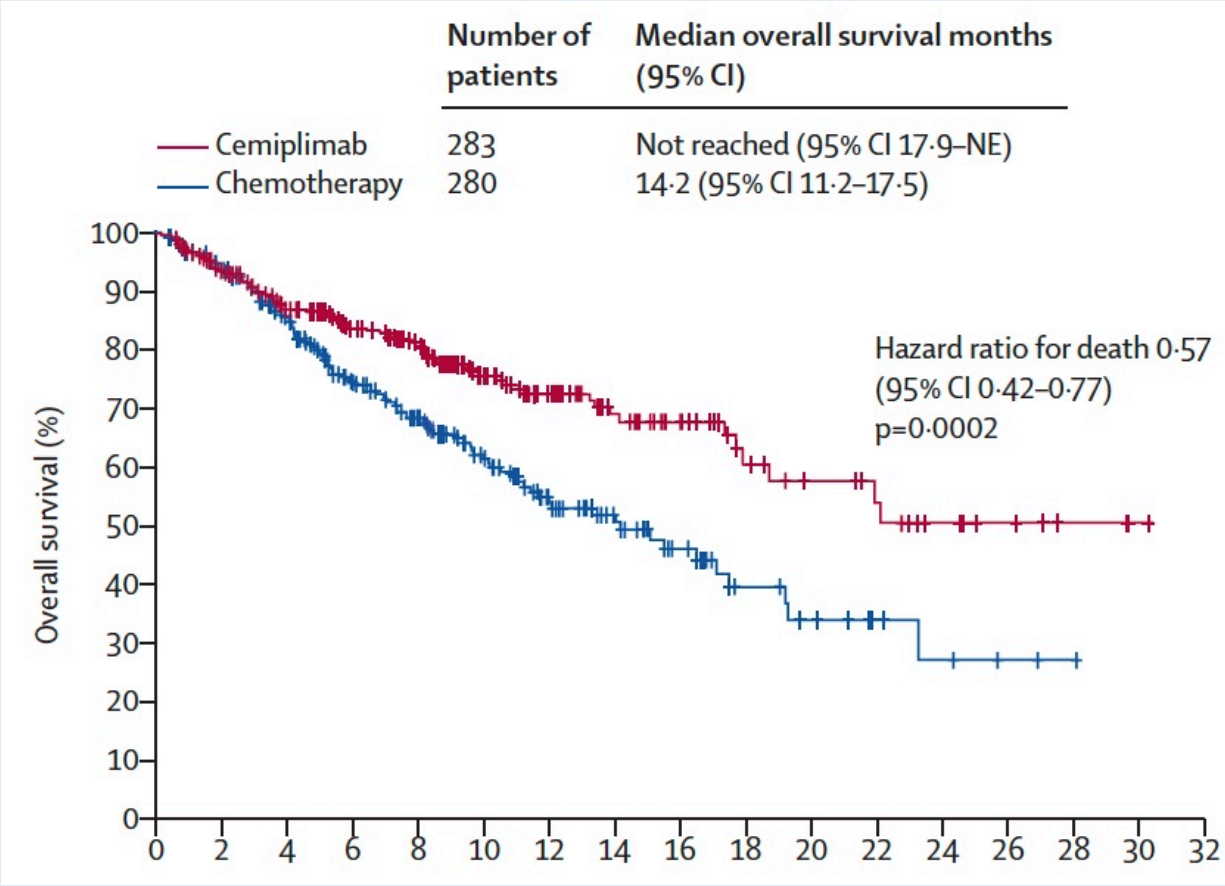
www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-cemiplimab-rwlc-non-small-cell-lung-cancer-high-pd-l1-expression

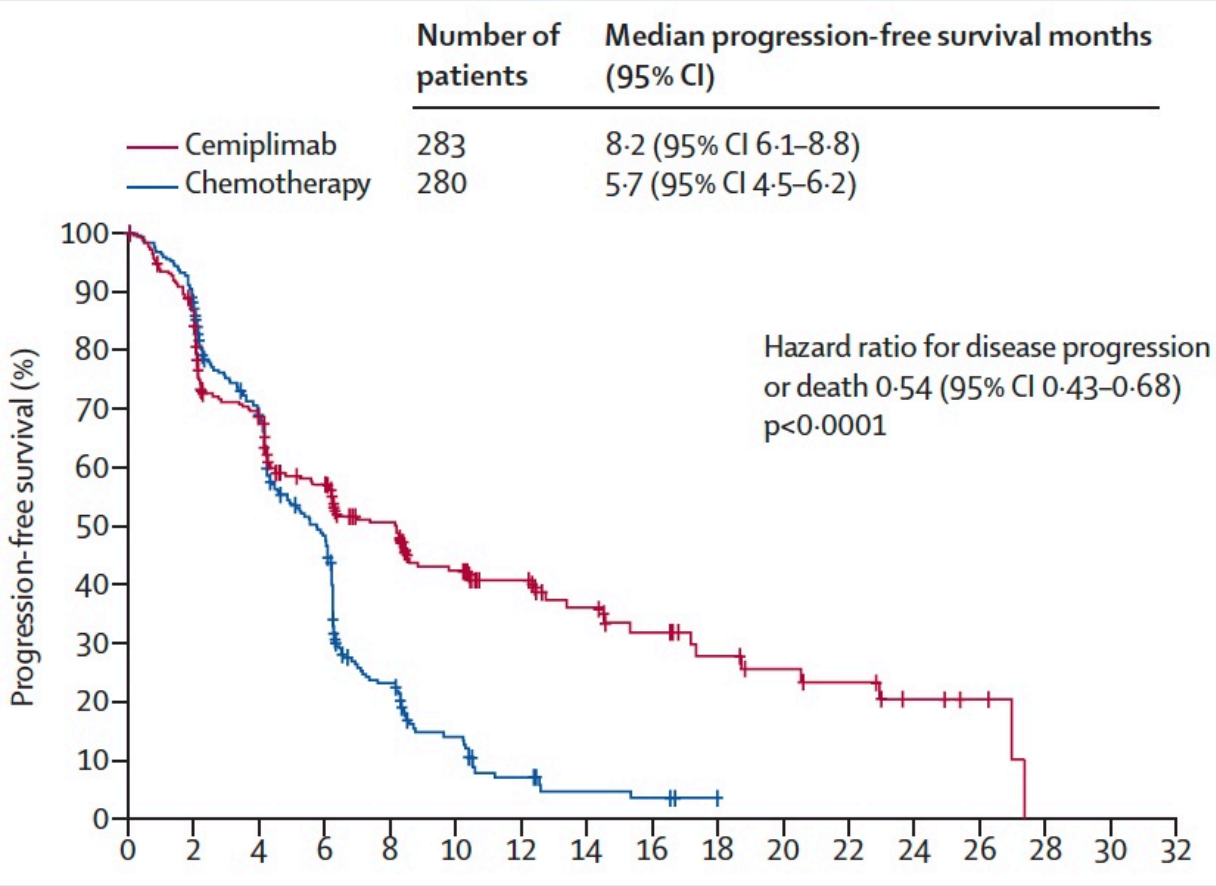
Lancet 2021;397(10274):592-604.

Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial

Ahmet Sezer, Saadettin Kilickap, Mahmut Gümüş, Igor Bondarenko, Mustafa Özgüroğlu, Miranda Gogishvili, Haci M Turk, Irfan Cicin, Dmitry Bentsion, Oleg Gladkov, Philip Clingan, Virote Sriuranpong, Naiyer Rizvi, Bo Gao, Siyu Li, Sue Lee, Kristina McGuire, Chieh-I Chen, Tamta Makharadze, Semra Paydas, Marina Nechaeva, Frank Seebach, David M Weinreich, George D Yancopoulos, Giuseppe Gullo, Israel Lowy, Petra Rietschel

Overall and Progression-Free Survival with First-Line Cemiplimab versus Chemotherapy





Sezer A et al. *Lancet* 2021;397(10274):592-604.

Agenda

- Case 1: A 52-year-old woman with NSCLC with an EGFR exon 19 mutation
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- Case 4: A 60-year-old man with newly diagnosed metastatic NSCLC with an ALK rearrangement
- Case 5: A 46-year-old woman with metastatic NSCLC with an EGFR exon 20 tumor mutation
  - Key Recent Data Sets – EXCLAIM, CHRYSALIS trials

Case Presentation – A 64-year-old woman with metastatic NSCLC with a HER2 mutation and PD-L1 40%

- Diagnosed with Stage IIIA NSCLC
  - PD-L1: 40%
- Concurrent carboplatin/paclitaxel + RT → Left VATS pneumonectomy
- Consolidation durvalumab → disease progression
- Carboplatin/pemetrexed/pembrolizumab – discontinued due to tolerability issues
- T-DM1 → discontinued due to neuropathy
- Trastuzumab deruxtecan

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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2021 ASCO ANNUAL MEETING

Abstract number: 8511

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

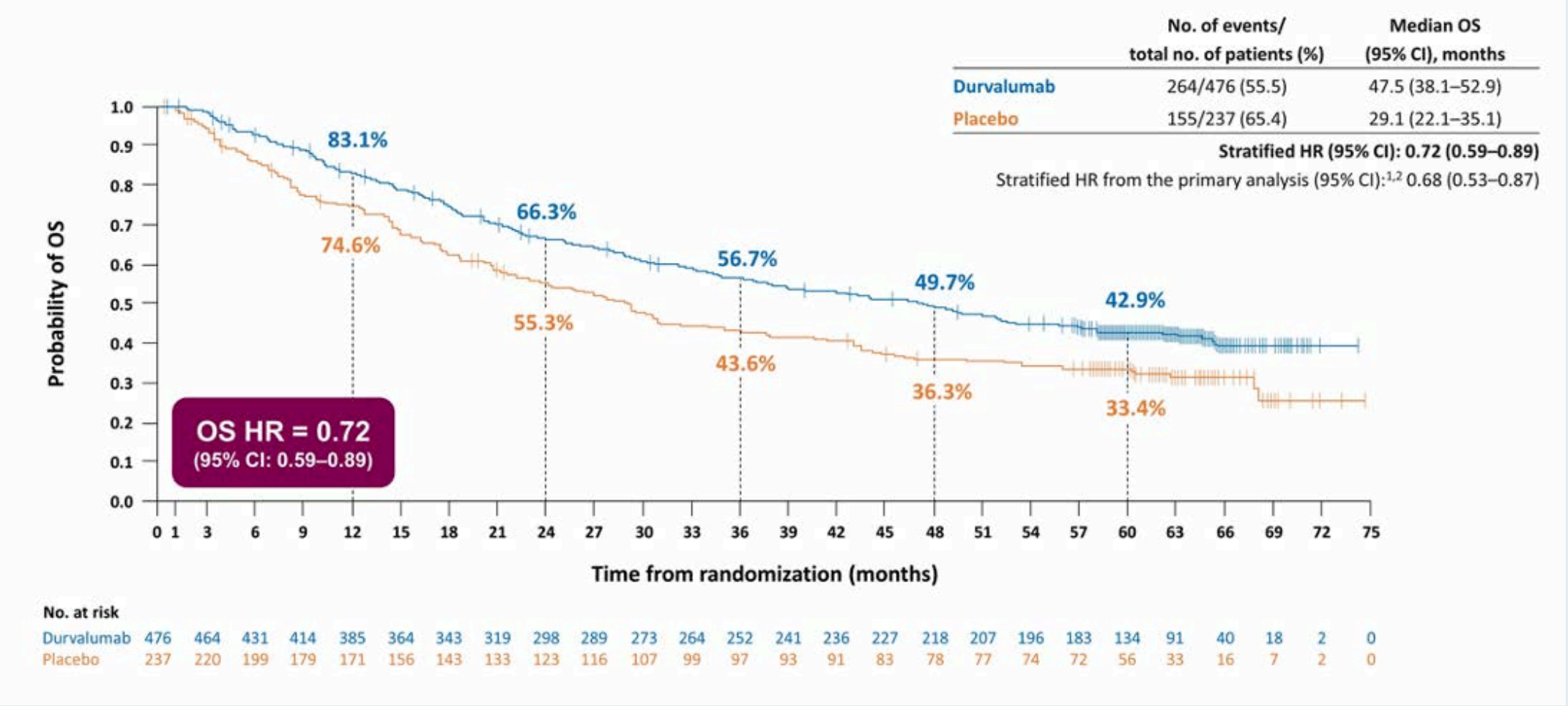
David R. Spigel,[1] Corinne Faivre-Finn,[2] Jhanelle E. Gray,[3] David Vicente,[4] David Planchard,[5] Luis Paz-Ares,[6] Johan F. Vansteenkiste,[7] Marina C. Garassino,[8,9] Rina Hui,[10] Xavier Quantin,[11] Andreas Rimner,[12] Yi-Long Wu,[13] Mustafa Özgüroğlu,[14] Ki H. Lee,[15] Terufumi Kato,[16] 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

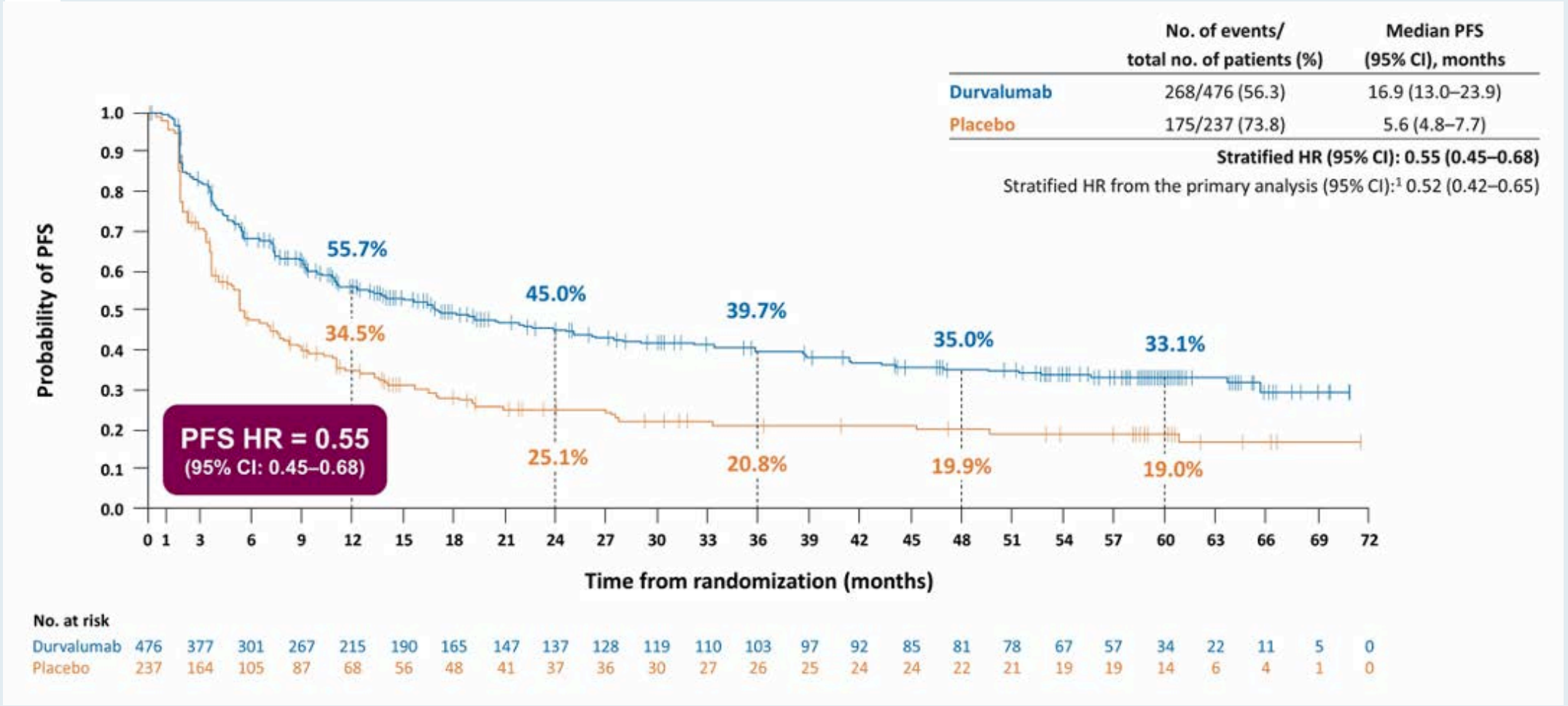
RTP RESEARCH TO PRACTICE

PACIFIC: 5-Year Overall Survival



Spigel DR et al. ASCO 2021;Abstract 8511.

PACIFIC: 5-Year Progression-Free Survival



Spigel DR et al. ASCO 2021;Abstract 8511.

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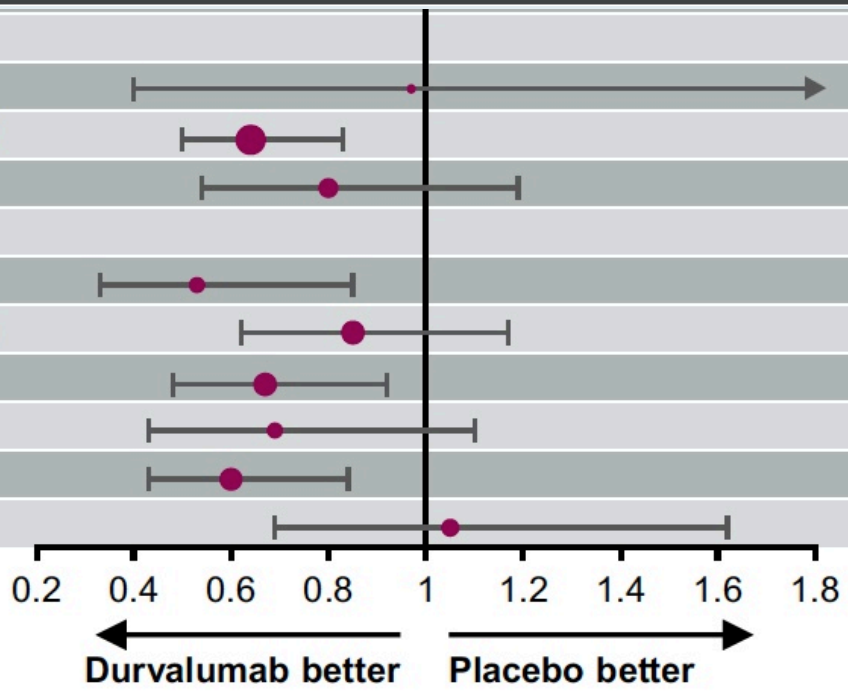
PACIFIC: 4-Year Overall Survival by EGFR and PD-L1 Status

	No. of events / No. of patients (%)		Unstratified HR (95% CI)
	Durvalumab	Placebo	
***EGFR* mutation**			
Positive	17/29 (58.6%)	7/14 (50.0%)	0.97 (0.40–2.33)
Negative	156/317 (49.2%)	105/165 (63.6%)	0.64 (0.50–0.83)
Unknown	74/130 (56.9%)	37/58 (63.8%)	0.80 (0.54–1.19)
PD-L1 status			
≥25%	50/115 (43.5%)	26/44 (59.1%)	0.53 (0.33–0.85)
<25%	102/187 (54.5%)	62/105 (59.0%)	0.85 (0.62–1.17)
Unknown	95/174 (54.6%)	61/88 (69.3%)	0.67 (0.48–0.92)
1–24% (post hoc analysis)	47/97 (48.5%)	28/47 (59.6%)	0.69 (0.43–1.10)
≥1% (post hoc analysis)	97/212 (45.8%)	54/91 (59.3%)	0.60 (0.43–0.84)
<1% (post hoc analysis)	55/90 (61.1%)	34/58 (58.6%)	1.05 (0.69–1.62)



Faivre-Finn C et al. *J Thorac Oncol* 2021;[Online ahead of print].

PACIFIC: Select Grade 3 or 4 Toxicity with Durvalumab After Chemoradiation for Stage III NSCLC

Adverse events (Grade 3 or 4)	Durvalumab (N = 475)	Placebo (N = 234)
Any Grade 3 or 4	29.9%	26.1%
Cough	0.4%	0.4%
Dyspnea	1.5%	2.6%
Diarrhea	0.6%	1.3%
Pneumonia	4.4%	3.8%
Anemia	2.9%	3.4%

Adverse events leading to discontinuation of treatment occurred in approximately 15.4% in the durvalumab group and 9.8% in the placebo group

Antonia SJ et al. *N Engl J Med* 2017;377(20):1919-29; *N Eng J Med* 2018;379(24):2342-50.

Trastuzumab Deruxtecan in HER2-Mutated Metastatic Non-Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01[1]

Trastuzumab Deruxtecan in HER2-Overexpressing Metastatic Non-Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01[2]

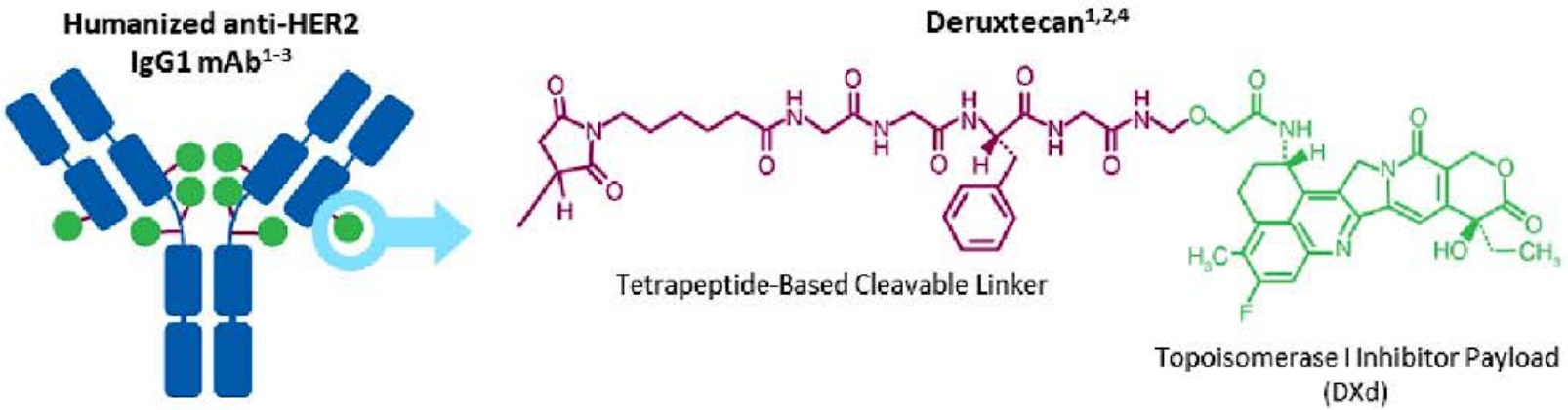
[1] Smit EF et al.
IASLC/WCLC 2020;Abstract MA11.03.

[2] Nakagawa K et al.
IASLC/WCLC 2020;Abstract OA04.05.

Antibody-Drug Conjugate
Trastuzumab Deruxtecan (T-DXd)

T-DXd is an ADC with 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker

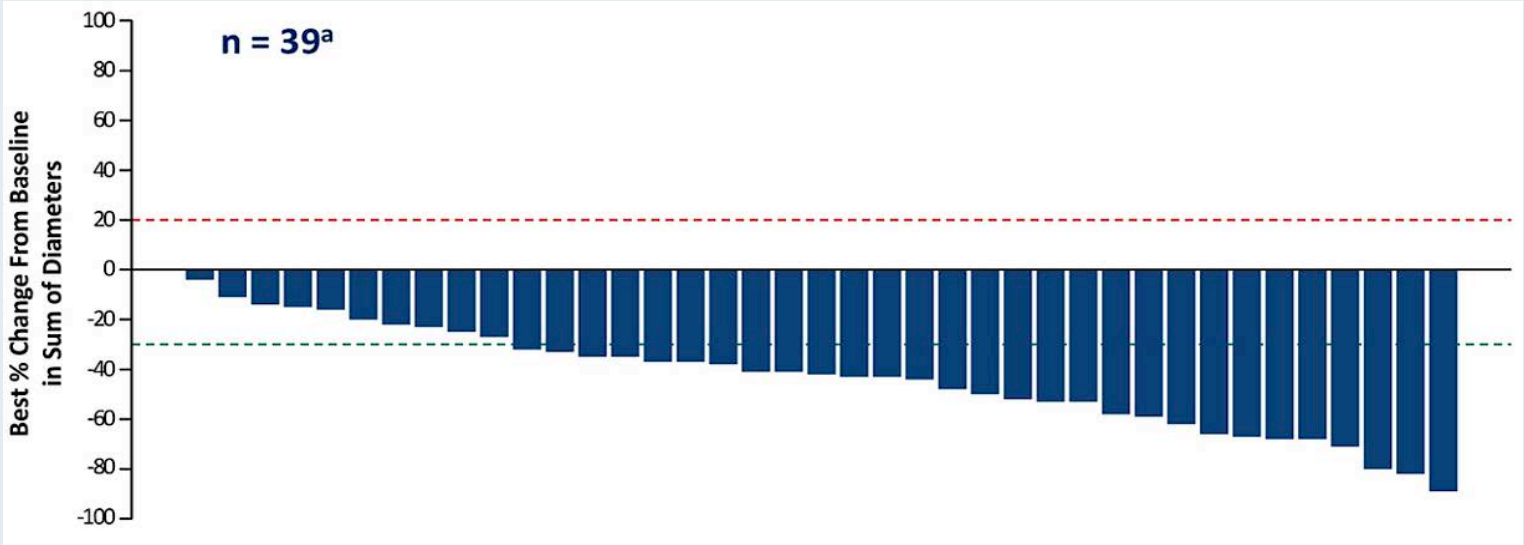


Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug to antibody ratio ≈ 8
Payload with short systemic half-life
Stable linker-payload
Tumor-selective cleavable linker
Membrane-permeable payload

Smit EF et al. ASCO 2020;Abstract 9504.

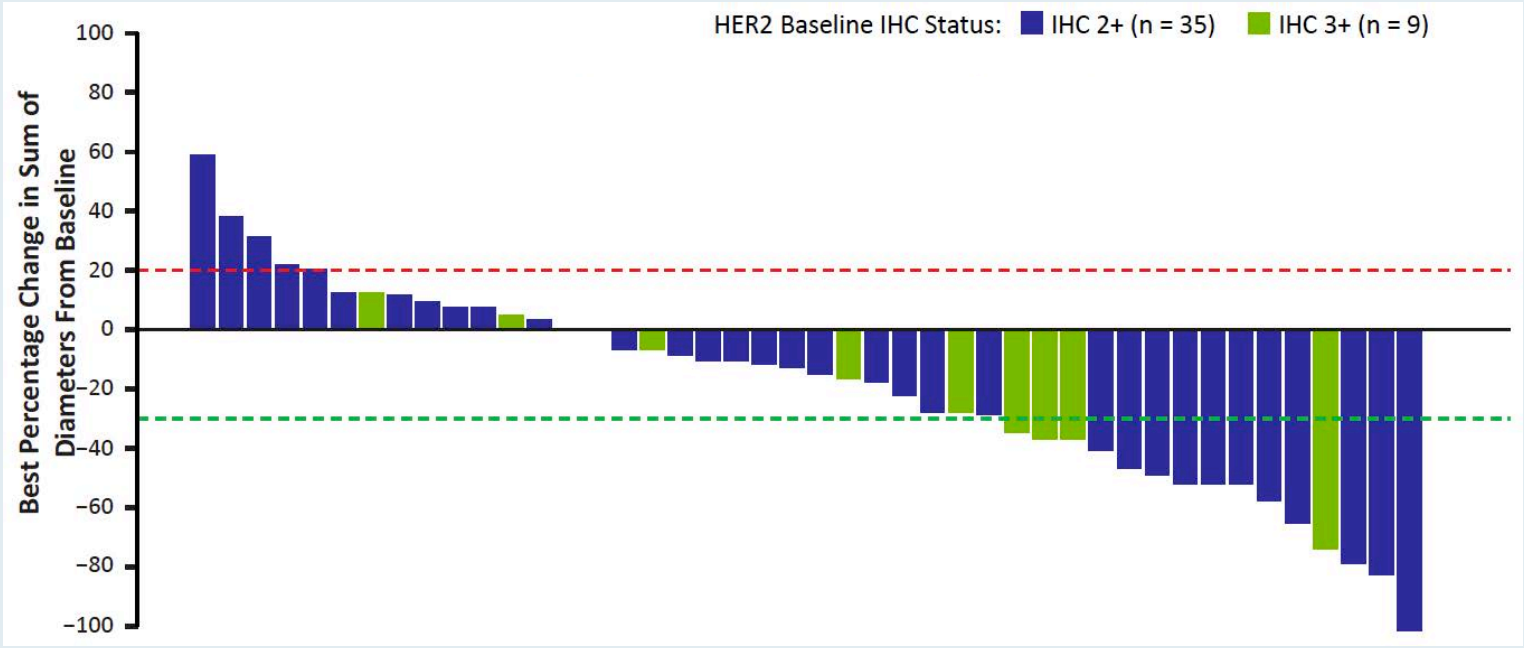
DESTINY-Lung01: Best Percentage Change in Tumor Size with T-DXd in NSCLC with HER2 Mutation versus Overexpression

Mutation



Confirmed ORR = 61.9%
DCR = 90.5%
Median DoR = not reached
Median PFS = 14.0 months

Overexpression



Confirmed ORR = 24.5%
DCR = 69.4%
Median DoR = 6.0 months
Median PFS = 5.4 months

Smit EF et al. IASLC/WCLC 2020;Abstract MA11.03; Nakagawa K et al. IASLC/WCLC 202o;Abstract OA04.05.

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  - Key Recent Data Sets – EXCLAIM, CHRYSALIS trials

Case Presentation – A 60-year-old man with newly diagnosed metastatic NSCLC with an ALK rearrangement

- First-line crizotinib → disease progression after ~1.5 years
- Second-line lorlatinib
- Third-line carboplatin/pemetrexed/pembrolizumab
- Fourth-line brigatinib

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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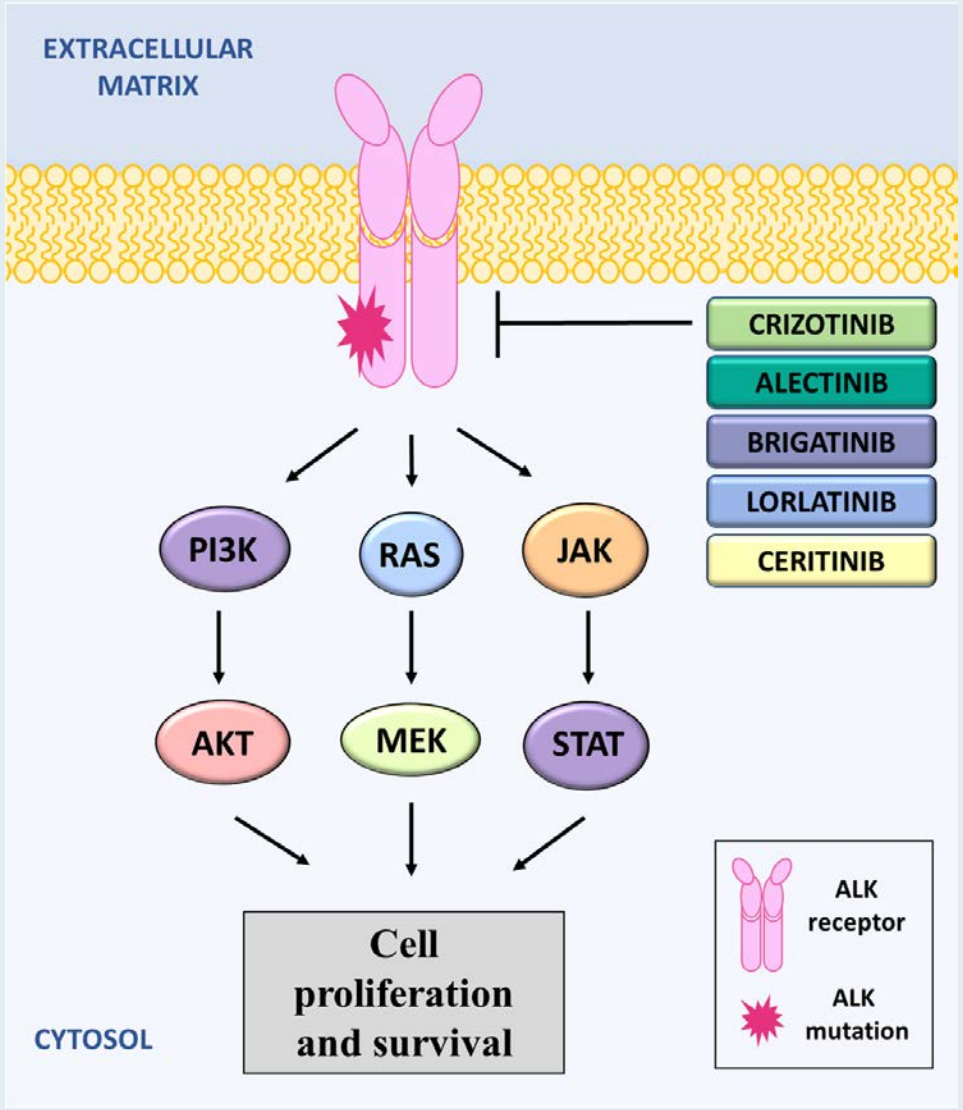
Mechanism of Action of ALK Inhibitors



3-13% of NSCLCs

Seebacher NA et al. JECCR 2019;38(156).

Timeline of FDA Approvals for ALK TKIs

Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-253.

RTP RESEARCH TO PRACTICE

FDA Expands Lorlatinib Approval to Front-Line Treatment of Metastatic NSCLC with ALK Fusion

Press Release – March 3, 2021

"The Food and Drug Administration granted regular approval to lorlatinib for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive, detected by an FDA-approved test. The FDA also approved the Ventana ALK (D5F3) CDx Assay (Ventana Medical Systems, Inc) as a companion diagnostic for lorlatinib.

Lorlatinib received accelerated approval in November 2018 for the second- or third-line treatment of ALK-positive metastatic NSCLC.

This current approval is based on data from Study B7461006 (NCT03052608), a randomized, multicenter, open-label, active-controlled trial conducted in 296 patients with ALK-positive metastatic NSCLC who had not received prior systemic therapy for metastatic disease. Patients were required to have ALK-positive tumors detected by the VENTANA ALK (D5F3) CDx assay. Patients were randomized 1:1 to receive lorlatinib 100 mg orally once daily (n=149) or crizotinib 250 mg orally twice daily (n=147). Study B7461006 demonstrated an improvement in progression-free survival (PFS) as assessed by blinded independent central review (BICR), with a hazard ratio of 0.28 (95% CI: 0.19, 0.41; p<0.0001)."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-lorlatinib-metastatic-alk-positive-nsclc?utm_medium=email&utm_source=govdelivery

RTP RESEARCH TO PRACTICE

Activity of ALK TKIs in the First-Line Setting for Advanced NSCLC with ALK Rearrangement

ALK TKI	Median PFS	ORR	Intracranial response
Crizotinib	10.9 mo	74%	NA
Ceritinib	16.6 mo	72.5%	72.7%
Alectinib	34.8 mo	82.9%	82.9%
Brigatinib	29.4 mo	71%	78%
Lorlatinib	Not reached	90%	66.7%
Ensartinib	26.2 mo	80%	64.3%

Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-253.

RTP RESEARCH TO PRACTICE

Common and Unique Adverse Effects of ALK TKIs

ALK TKI	Most frequent adverse effects
Crizotinib	Vision disorders, nausea, diarrhea, vomiting, edema, constipation, elevated transaminases, fatigue, decreased appetite, upper respiratory infection, dizziness, neuropathy
Ceritinib	Diarrhea, nausea, vomiting, fatigue, abdominal pain, decreased appetite, weight loss
Alectinib	Constipation, fatigue, edema, myalgia, anemia
Brigatinib	Diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting, dyspnea
Lorlatinib	Hypercholesterolemia, hypertriglyceridemia, edema, peripheral neuropathy, weight gain, cognitive effects, fatigue, dyspnea, arthralgia, diarrhea
Ensartinib	Rash, nausea, pruritus, vomiting

Crizotinib PI, rev 1/2021; Ceritinib PI, rev 3/2019; Alectinib PI, rev 1/2021; Brigatinib PI, rev 5/2020; Lorlatinib PI, rev 3/2021
Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-253; Gristina V et al. *Pharmaceuticals* 2020;13:474.

Agenda

- Case 1: A 52-year-old woman with NSCLC with an EGFR exon 19 mutation
  - Key Recent Data Sets – ADAURA, FLAURA, BLOOM trials
- Case 2: A 64-year-old man with newly diagnosed metastatic adenocarcinoma of the lung – PD-L1 95%
  - Key Recent Data Sets – KEYNOTE-001 trial, Study 1624
- Case 3: A 64-year-old woman with metastatic NSCLC with a HER2 mutation and PD-L1 40%
  - Key Recent Data Sets – PACIFIC, DESTINY-Lung01 trials
- Case 4: A 60-year-old man with newly diagnosed metastatic NSCLC with an ALK rearrangement
- Case 5: A 46-year-old woman with metastatic NSCLC with an EGFR exon 20 tumor mutation
  - Key Recent Data Sets – EXCLAIM, CHRYSALIS trials

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Case Presentation – A 46-year-old woman with metastatic NSCLC with an EGFR exon 20 tumor mutation

- Originally treated with osimertinib by another oncologist
- Treated with carboplatin/pemetrexed upon disease progression
- Patient presents to Cleveland Clinic for second opinion
- NGS: EGFR exon 20 tumor mutation

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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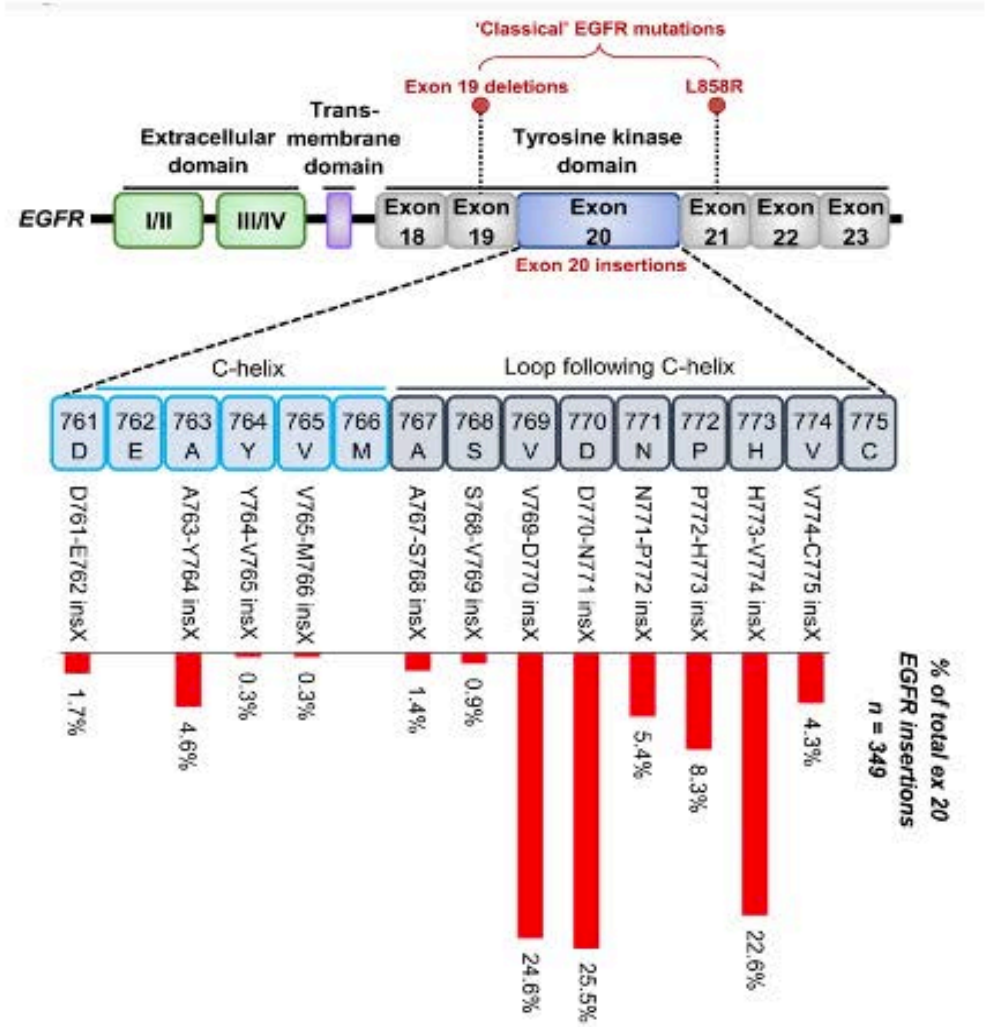
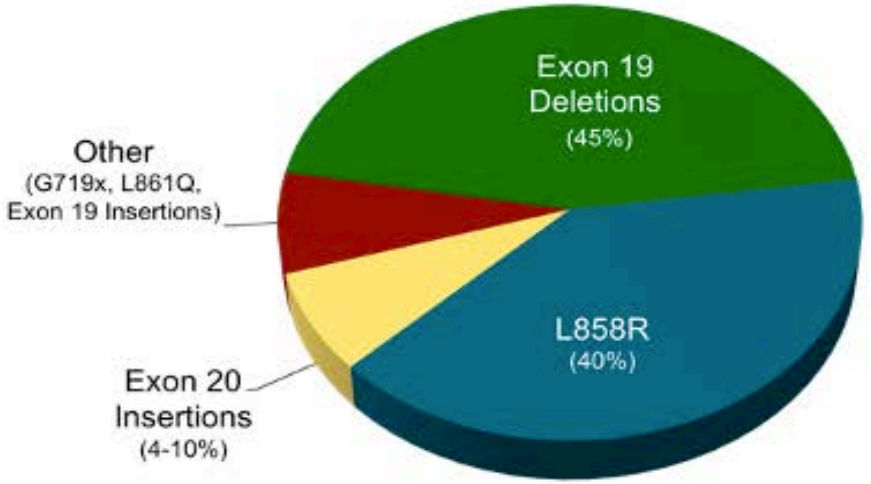
Frequency of EGFR Exon 20 Mutations





Exon 20 NSCLC: US and China				
		Exon 20 Frequency	Total Number of NSCLC Patients/year	
United States	EGFR HER2	2.1% 1.5%	3.6%	7700
China	EGFR HER2	2.4% 3.9%	6.3%	41100

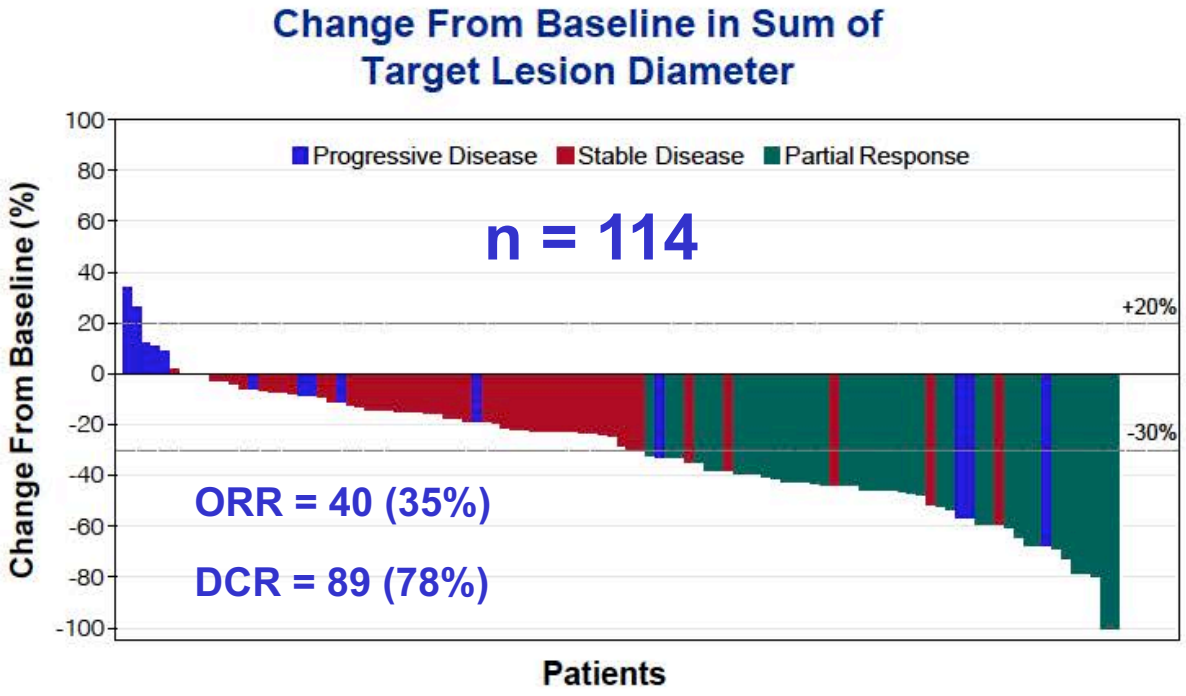
Courtesy of Zosia Piotrowska, MD.

Emerging Targeted Therapies for EGFR Exon 20 Mutations

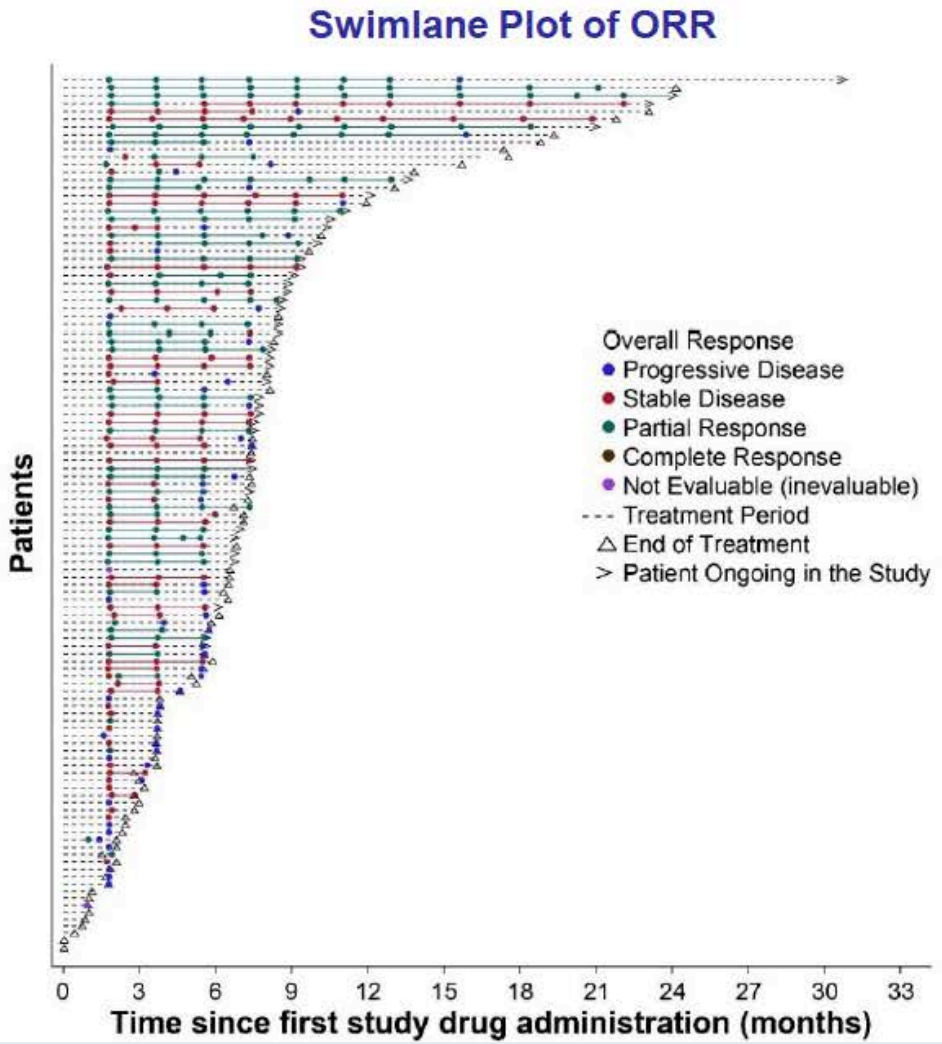
Drug	MOA	N	ORR	mPFS	Major toxicities	Discont due to toxicities	FDA status re exon 20
Poziotinib[1,2]	TKI	115	15%	4.2 mo	Diarrhea Rash	12%	Fast track designation March 2021
Mobocertinib[3,4,5]	TKI	114	35%	7.3 mo	Diarrhea Rash Nausea	14%	Breakthrough therapy designation April 2020
Amivantamab[6]	EGFR/ MET Ab	81	40%	8.3 mo	Rash Infusion reaction Paronychia	4%	FDA accelerated approval May 2021
Osimertinib[7]	TKI	17	24%	9.6 mo	Diarrhea Rash Platelets	6%	No indication in exon 20
CLN-081[8]	TKI	22	35%	NR	Rash Stomatitis	0%	Investigational

1. Le X. AACR 2020, 2. Socinski M. ESMO 2020; 3. Riely G. ESMO 2020; 4. Zhou C. IASLC 2020; 5. Zhou C. IASLC/WCLC 2020. 6. Sabari JK. IASLC WCLC 2020; 7. Piotrowska Z. ASCO 2020; 8. Piotrowska Z. ESMO 2020.

EXCLAIM: Mobocertinib in Platinum-Pretreated NSCLC with EGFR Exon 20 Insertions



- 94 patients (82%) had a reduction from baseline in the sum of target lesion diameter



ORR, objective response rate; PPP, platinum-pretreated patients

Zhou C et al. IASLC/WCLC 2020;Abstract OA04.03

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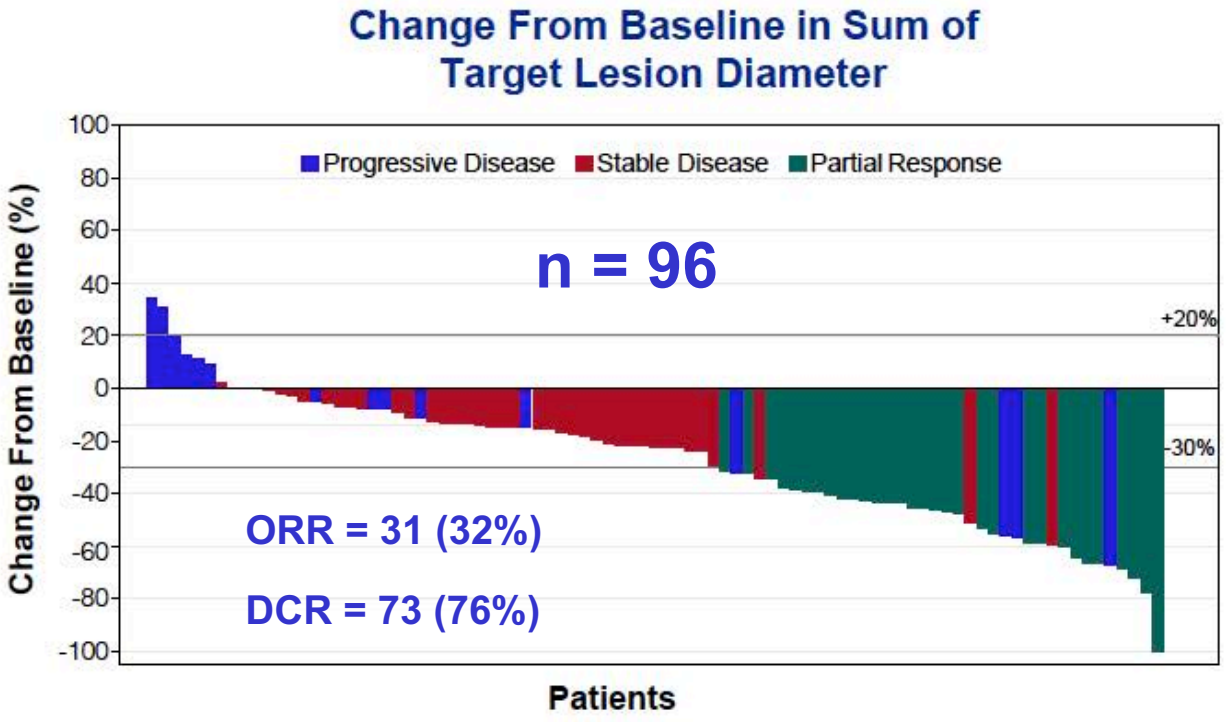
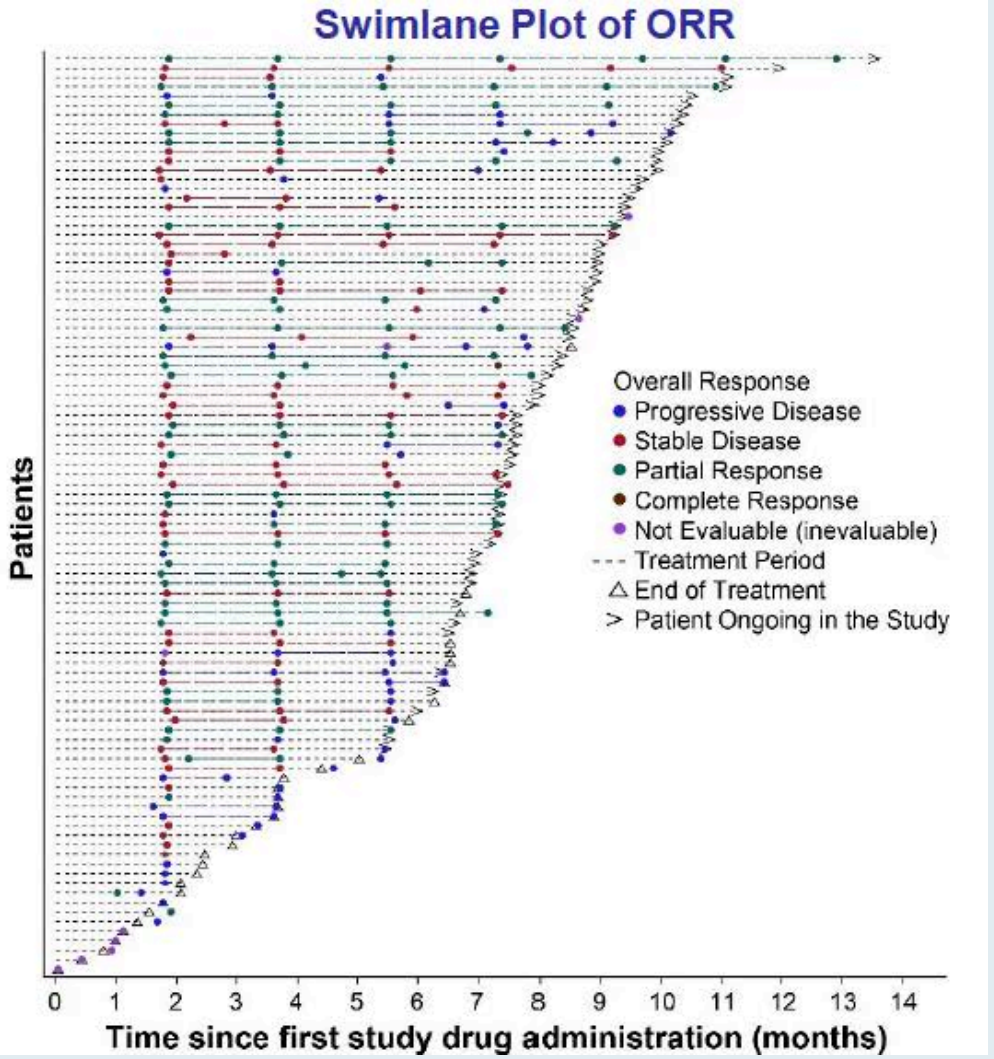
Mobocertinib Resulted in Reductions in Target Lesion Volume in EXCLAIM Cohort





- 77 patients (80%) had a reduction from baseline in the sum of target lesion diameter

ORR, objective response rate

Zhou C et al. IASLC/WCLC 2020;Abstract OA04.03

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FDA Grants Accelerated Approval to Amivantamab-vmjw for Metastatic NSCLC with EGFR Exon 20 Insertion Mutations

Press Release – May 21, 2021

"The Food and Drug Administration granted accelerated approval to amivantamab-vmjw, a bispecific antibody directed against epidermal growth factor (EGF) and MET receptors, for adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. FDA also approved the Guardant360® CDx as a companion diagnostic for amivantamab-vmjw.

Approval was based on CHRYSALIS, a multicenter, non-randomized, open label, multicohort clinical trial (NCT02609776) which included patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. Efficacy was evaluated in 81 patients with advanced NSCLC with EGFR exon 20 insertion mutations whose disease had progressed on or after platinum-based chemotherapy. Patients received amivantamab-vmjw once weekly for 4 weeks, then every 2 weeks thereafter until disease progression or unacceptable toxicity.

The main efficacy outcome measures were overall response rate (ORR) according to RECIST 1.1 as evaluated by blinded independent central review (BICR) and response duration. The ORR was 40% with a median response duration of 11.1 months."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-amivantamab-vmjw-metastatic-non-small-cell-lung-cancer

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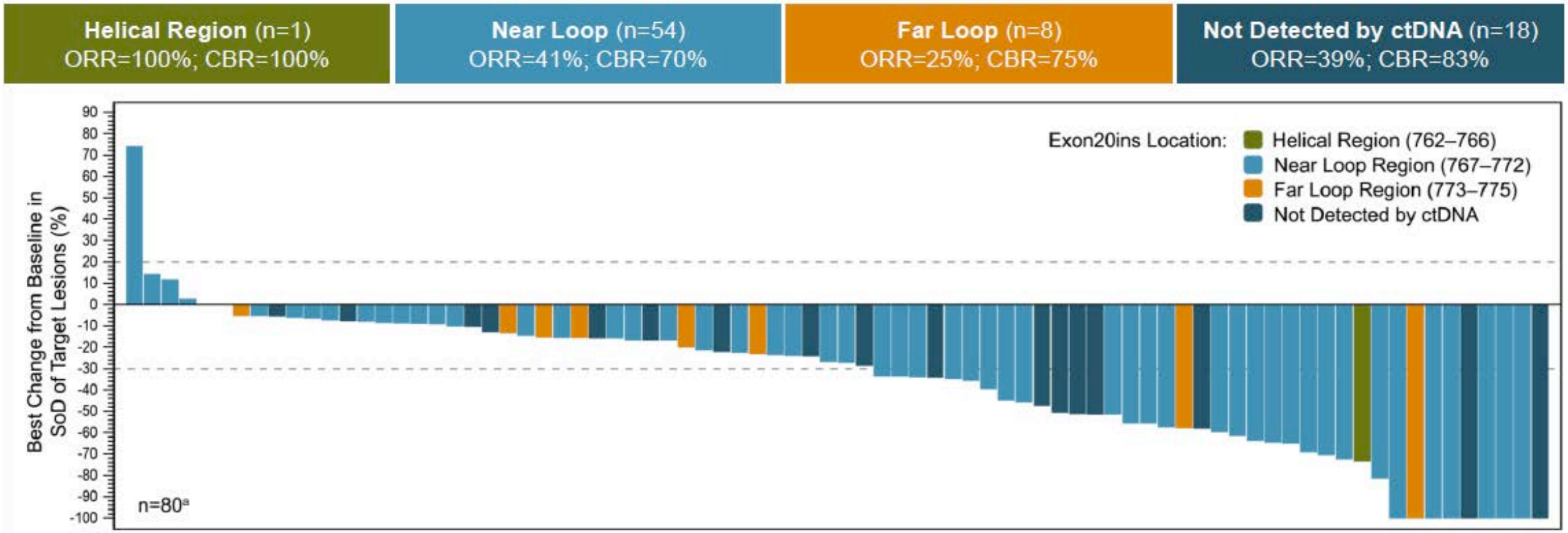
CHRYSALIS: Best ORR with Amivantamab by Insertion Region of Exon 20



25 distinct Exon20ins variants identified by NGS of ctDNA (Guardant360®) from 63 evaluable patient samples

Sabari JK et al. IASLC WCLC 2020;Abstract OA04.04.

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A Conversation with the Investigators: Hormonal Therapy for Prostate Cancer

Monday, July 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Simon Chowdhury, MD, PhD
Tanya B Dorff, MD
Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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