What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Non-Small Cell Lung Cancer

Thursday, April 28, 2022
6:00 PM – 8:00 PM PT

Faculty

Edward B Garon, MD, MS
Kelly EH Goodwin, MSN, RN, ANP-BC
Tara Plues, APRN, MSN
Anne S Tsao, MD, MBA

Moderator

Neil Love, MD

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Faculty

Edward B Garon, MD, MS
Professor
Director, Thoracic Oncology Program
Director, Signal Transduction and Therapeutics Research Program
David Geffen School of Medicine at UCLA
Jonsson Comprehensive Cancer Center
Los Angeles, California

Anne S Tsao, MD, MBA
Vice President, Faculty and Academic Affairs
Professor, Thoracic/Head and Neck Medical Oncology
Clinical Medical Director ad Interim, Thoracic and Orthopaedic Center
Director, Mesothelioma Program
The University of Texas MD Anderson Cancer Center
Houston, Texas

Kelly EH Goodwin, MSN, RN, ANP-BC
Thoracic Cancer Center
Massachusetts General Hospital
Boston, Massachusetts

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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

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Dr Garon — Disclosures

Consulting Agreements	ABL Bio, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Dracen Pharmaceuticals, Eisai Inc, EMD Serono Inc, Gilead Sciences Inc, GlaxoSmithKline, Merck, Natera Inc, Novartis, Personalis Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Shionogi Inc, Xilio Therapeutics
Contracted Research	ABL Bio, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Dynavax Technologies, EMD Serono Inc, Genentech, a member of the Roche Group, Iovance Biotherapeutics, Lilly, Merck, Mirati Therapeutics, Neon Therapeutics, Novartis

Ms Goodwin — Disclosures

No relevant conflicts of interest to disclose

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Ms Plues — Disclosures

No relevant conflicts of interest to disclose

Dr Tsao — Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, EMD Serono Inc, Epizyme Inc, Genentech, a member of the Roche Group, Huron, Lilly, Merck, Novartis, Roche Laboratories Inc, Seagen Inc, SELLAS Life Sciences, Takeda Pharmaceuticals USA Inc
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Research To Practice CME Planning Committee Members, Staff and Reviewers

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Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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"What I Tell My Patients"
14th Annual RTP-ONS NCPD Symposium Series
ONS Congress, Anaheim, California — April 27 - May 1, 2022

Thursday April 28	**Prostate Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Non–Small Cell Lung Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Hepatobiliary Cancers 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Friday April 29	**Small Cell Lung Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Acute Myeloid Leukemia and Myelodysplastic Syndromes 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Saturday April 30	**Cervical and Endometrial Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Bladder Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

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What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

An NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Prostate Cancer

Thursday, April 28, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Kathy D Burns, RN, MSN, AGACNP-BC, OCN
Robert Dreicer, MD, MS
Sandy Srinivas, MD
Ronald Stein, JD, MSN, NP-C, AOCNP

Non-Small Cell Lung Cancer

Thursday, April 28, 2022
6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty
Edward B Garon, MD, MS
Kelly EH Goodwin, MSN, RN, ANP-BC
Tara Plues, APRN, MSN
Anne S Tsao, MD, MBA

Ovarian Cancer

Thursday, April 28, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Jennifer Filipi, MSN, NP
Kathleen N Moore, MD, MS
Krishnansu S Tewari, MD
Deborah Wright, MSN, APRN, AGCNS-BC

Hepatobiliary Cancers

Thursday, April 28, 2022
8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty
Richard S Finn, MD
Amanda K Wagner, APRN-CNP, AOCNP

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

An NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Small Cell Lung Cancer

Friday, April 29, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Marianne J Davies, DNP, MSN, RN, APRN
Matthew Gubens, MD, MS
Lowell L Hart, MD
Chaely J Medley, MSN, AGNP

Breast Cancer

Friday, April 29, 2022
6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty
Jamie Carroll, APRN, MSN, CNP
Sara A Hurvitz, MD
Kelly Leonard, MSN, FNP-BC
Hope S Rugo, MD

Chronic Lymphocytic Leukemia

Friday, April 29, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Lesley Camille Ballance, MSN, FNP-BC
Amy Goodrich, CRNP
Anthony R Mato, MD, MSCE
Susan O'Brien, MD

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Friday, April 29, 2022
8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty
Ilene Galinsky, NP
Eunice S Wang, MD

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

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Cervical and Endometrial Cancer

Saturday, April 30, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Paula J Anastasia, MN, RN, AOCN
Robert L Coleman, MD
David M O'Malley, MD
Jaclyn Shaver, MS, APRN, CNP, WHNP

Bladder Cancer

Saturday, April 30, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Monica Averia, MSN, AOCNP, NP-C
Shilpa Gupta, MD
Brenda Martone, MSN, NP-BC, AOCNP
Sumanta Kumar Pal, MD

Join Us After ONS for Our Series Continuation

What I Tell My Patients —
A 2-Part NCPD Webinar Series

Hodgkin and Non-Hodgkin Lymphomas

Date and time to be announced

Gastroesophageal Cancers

Wednesday, May 18, 2022

5:00 PM – 6:00 PM ET

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Oncology Grand Rounds
2022 ONS Congress
Anaheim, California

Symposia Themes

Personalized oncology: Implementing an individualized oncologic strategy

- Tumor factors (eg, biomarkers, numeracy)
- Biopsychosocial factors (eg, adherence, available family support, comorbidities, mood)

Novel agents and treatment strategies

- The new-agents revolution (beginning of the end?)

The bond that heals (both ways)

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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?

How often do you wish you were in another line of work?

1. Never
2. A few times per year
3. Once a month
4. A few times per month
5. Once a week
6. A few times per week
7. Every day

Faculty

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Research To Practice
Miami, Florida

Tara Plues, APRN, MSN
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Cleveland, Ohio

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Agenda

Module 1 – Key Lung Cancer Diagnostic Tools

Module 2 – Targeted Therapy for Localized Disease

Module 3 – Targeted Treatment for Metastatic Disease

Module 4 – Immunotherapy for Localized Disease

Module 5 – Immunotherapy for Metastatic Disease

Agenda

Module 1 – Key Lung Cancer Diagnostic Tools

Module 2 – Targeted Therapy for Localized Disease

Module 3 – Targeted Treatment for Metastatic Disease

Module 4 – Immunotherapy for Localized Disease

Module 5 – Immunotherapy for Metastatic Disease

SELF-ASSESSMENT QUIZ

Which of the following assays is considered standard in the evaluation of newly diagnosed metastatic non-small cell lung cancer (NSCLC)?

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

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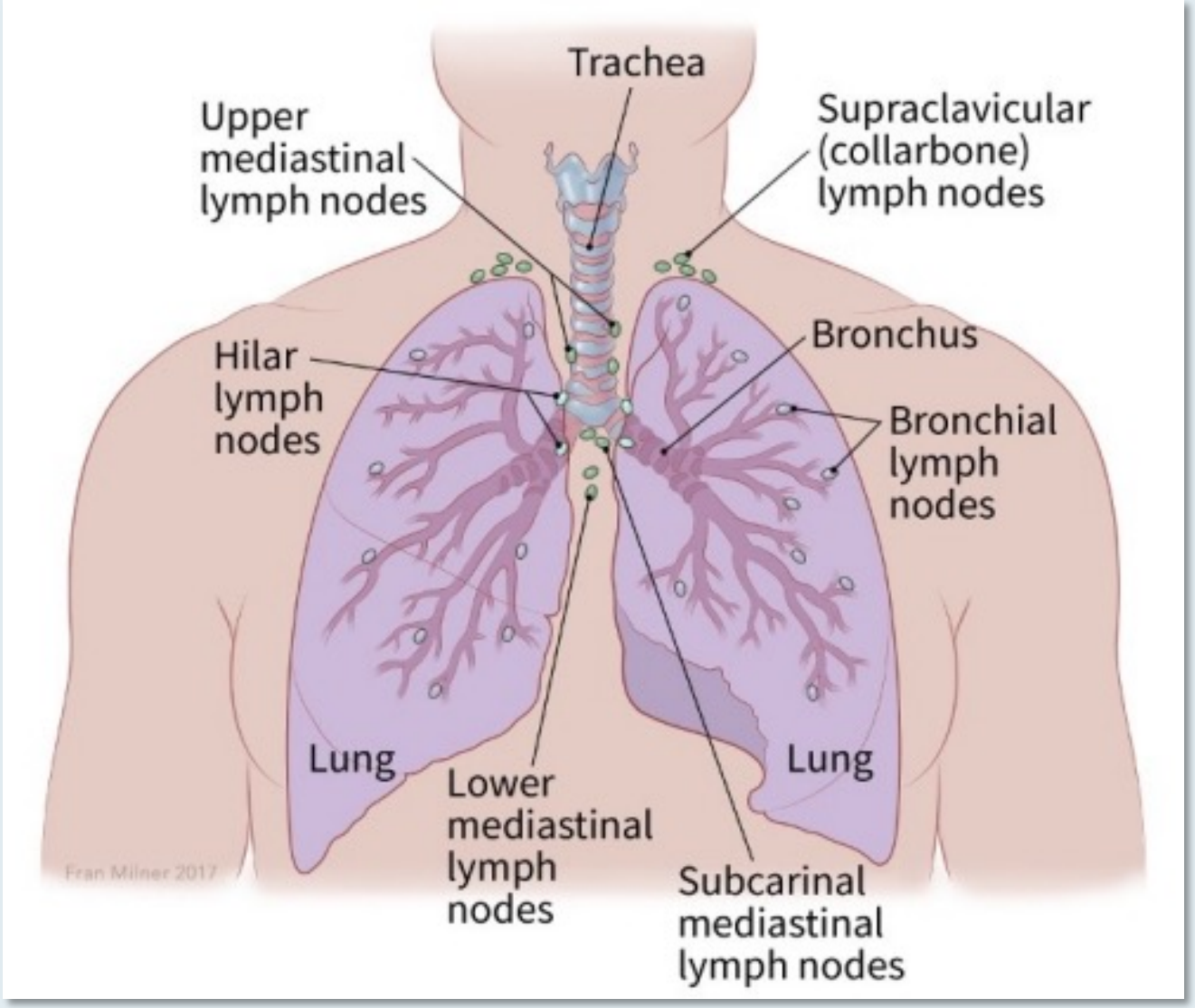
SELF-ASSESSMENT QUIZ

Targetable tumor-driver mutations in NSCLC generally occur in patients with…

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

Lung Anatomy: Distribution of Lymph Nodes



Stage Distribution at Diagnosis of Patients with Lung Cancer

SEER Analysis: (2004-2010, N = 344,797)

Stage at Diagnosis (AJCC, 7th Edition)	I	II	III	IV	Unknown
% of Patients	18%	7%	19%	49%	5%
Est No. of Patients in USA, 2019	41,067	15,971	43,349	111,794	11,408

Occult disease accounts for approximately 1.5%

Chen VW et al. *Cancer* 2014;120:3781-92. Siegel RL et al. *CA Cancer J Clin*. 2019 Jan;69(1):7-34.

Agenda

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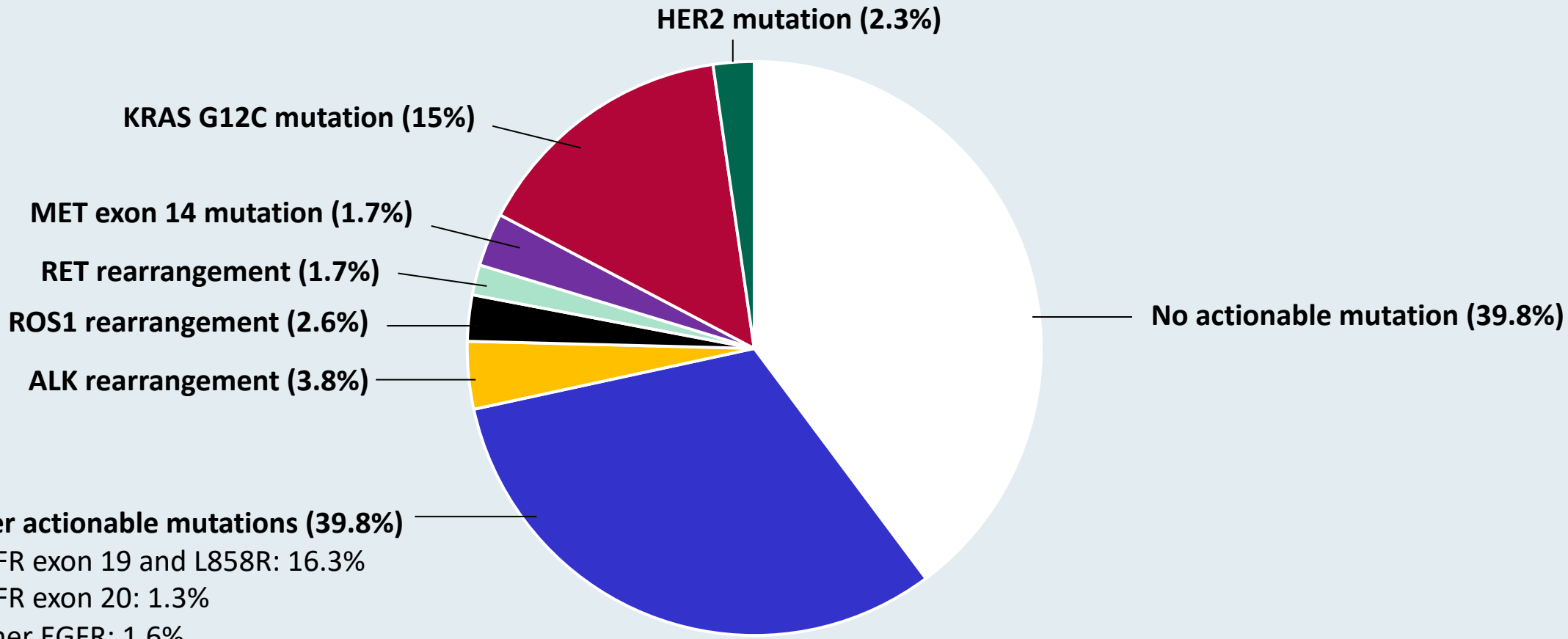
SELF-ASSESSMENT QUIZ

Patients with NSCLC who meet the eligibility criteria for adjuvant chemotherapy but have tumors with an activating EGFR tumor mutation receive…

1. Adjuvant chemotherapy
2. Adjuvant chemotherapy followed by osimertinib
3. Osimertinib
4. Other EGFR TKI (tyrosine kinase inhibitor)
5. I don’t know

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



Other actionable mutations (39.8%)
--EGFR exon 19 and L858R: 16.3%
--EGFR exon 20: 1.3%
--Other EGFR: 1.6%
--Other KRAS: 10.3%
--BRAF V600E: 2.1%
--NTRK rearrangement: 0.23%

Derived from: Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

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The NEW ENGLAND JOURNAL of MEDICINE

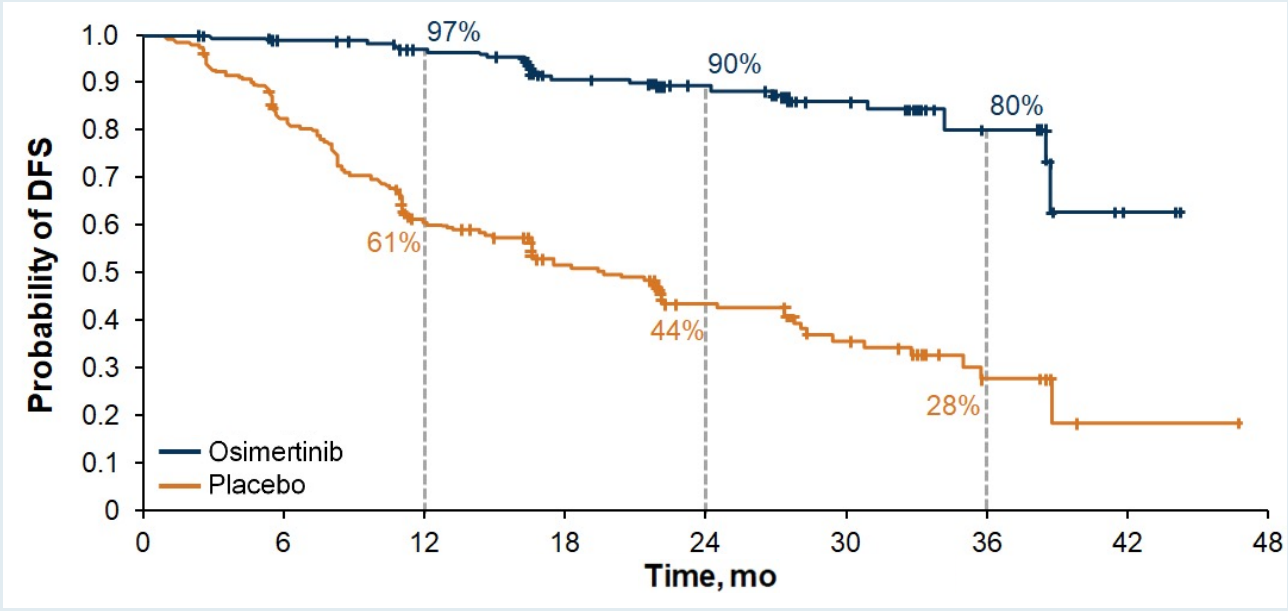
ESTABLISHED IN 1812 OCTOBER 29, 2020 VOL. 383 NO. 18

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*

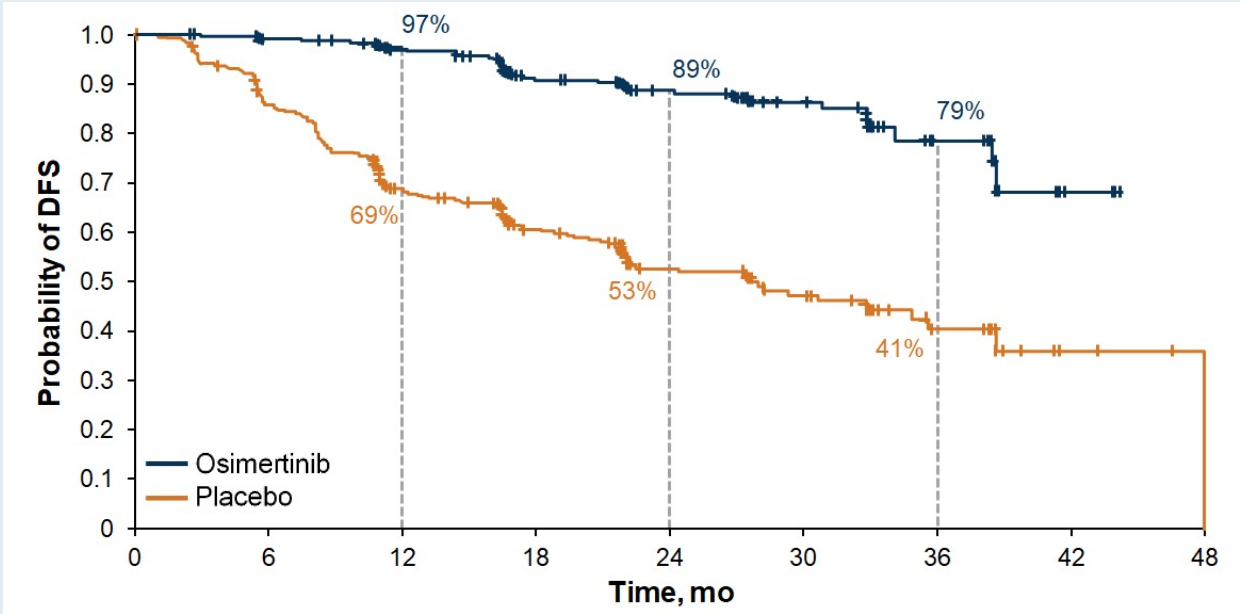
Phase III ADAURA Trial: Adjuvant Osimertinib

DFS: Stage II to IIIA Disease



HR = 0.17; *p* < .001 → 83% reduction in risk of disease recurrence or death

DFS: Stage IB to IIIA Disease



HR = 0.20; *p* < .001 → 80% reduction in risk of disease recurrence or death

DFS = disease-free survival

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

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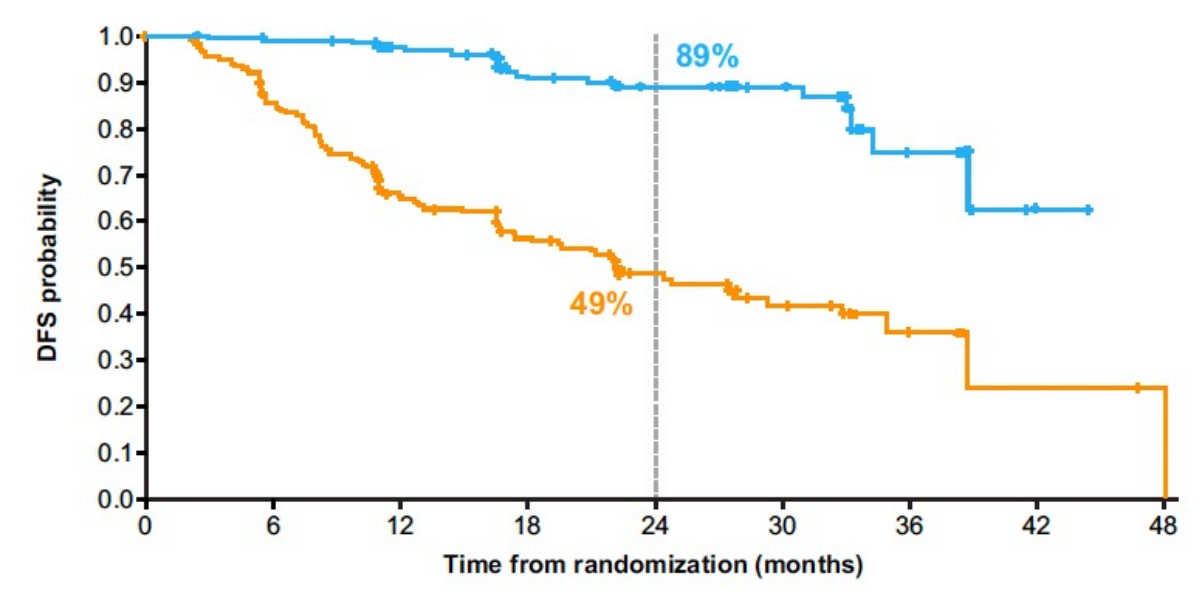
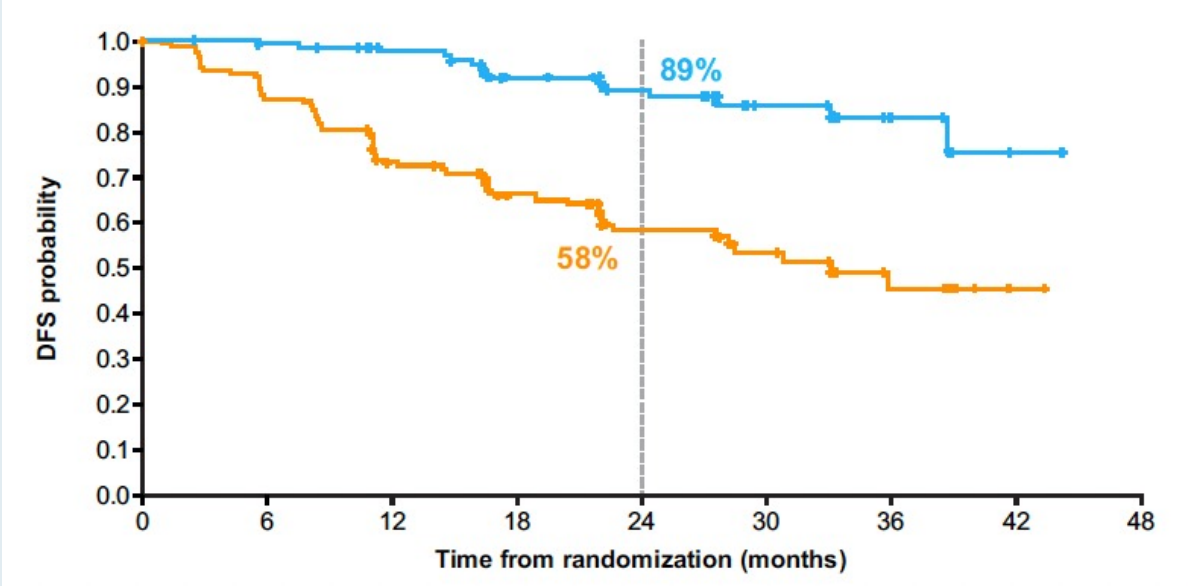
ADAURA: Updated DFS with Adjuvant Osimertinib for Patients Receiving and Not Receiving Adjuvant Chemotherapy

With Adjuvant Chemotherapy



Without Adjuvant Chemotherapy



Wu YL et al. *J Thorac Oncol* 2022;17(3):423-33.

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Questions — Edward B Garon, MD, MS

Patients with resected localized NSCLC and an EGFR activating mutation

- **How do you approach prevention and management of side effects and toxicity associated with targeted treatment in this situation?**

Commentary – Edward B Garon, MD, MS

Patients with resected localized NSCLC and an EGFR activating mutation

- **Reassure patients that the tolerability is generally better than chemotherapy (which they have generally received)**
- **Remember that patients don’t care about relative toxicity to drugs they don’t know (eg, erlotinib)**
- **Remind patients to discuss their toxicities, as issues with a daily drug can become annoying**
- **Explain that although the study treated for 3 years, they don’t make a 3 year commitment today**

Commentary – Edward B Garon, MD, MS

- **Clinical case**
- **Man in mid 40s with stage II (hilar lymph nodes) resected NSCLC**
- **Tolerated chemotherapy well**
- **Opted to receive adjuvant osimertinib subsequently**
- **Less than a year later, develops malignant pleural effusion**
- **Subsequently acknowledges stopping the drug 3 months prior**
- **Explains an increase in cost to him, although also notes minor toxicities**

Agenda

Module 1 – Key Lung Cancer Diagnostic Tools

Module 2 – Targeted Therapy for Localized Disease

Module 3 – Targeted Treatment for Metastatic Disease

- **EGFR activating mutations**
- EGFR exon 20 insertion mutations
- ALK rearrangements
- RET fusions
- KRAS G12C mutations
- HER2 mutations
- Other targets in NSCLC (MET, ROS1, BRAF, NTRK, NRG1)

Module 4 – Immunotherapy for Localized Disease

Module 5 – Immunotherapy for Metastatic Disease

SELF-ASSESSMENT QUIZ

Anti-PD-1/PD-L1 monotherapy yields very low response rates among patients with NSCLC and EGFR tumor mutations.

1. Agree
2. Disagree
3. I don’t know

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SELF-ASSESSMENT QUIZ

For patients with previously untreated NSCLC, an EGFR tumor mutation and multiple bilateral asymptomatic brain metastases that would require whole-brain radiation therapy, osimertinib is generally administered.

1. Agree
2. Disagree
3. I don’t know

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EGFR Targeted Therapy in Metastatic NSCLC

- Role of radiation therapy for brain metastases
- Evaluation of PD-L1 status and use of anti-PD-1/PD-L1 antibodies
- Management of side effects and toxicities with osimertinib
- Approach to patients who initially respond to osimertinib and then experience disease progression

Questions — Tara Plues, APRN, MSN

Patients with NSCLC who are about to begin targeted treatment

- **In general, what do you say to patients with NSCLC who are about to receive targeted treatment in terms of side effects/toxicities?**
- **What are some of the psychosocial issues that arise in this situation?**

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Commentary — Tara Plues, APRN, MSN

Patients with NSCLC who are about to begin targeted treatment

- **What do I say to patients with NSCLC who are about to receive targeted treatment in terms of side effects/toxicities?**
- **In general these medications are well tolerated. I tell them that this is an ideal situation, to target a known driver within the cancer. I assure them in our knowledge and ability to manage potential side effects. I advise them that the goal is tolerability. We will work at managing any side effects to the best of our ability and if we are unable to successfully do that we can talk about reducing the dose of the drug. Tolerability is just as important as efficacy.**

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Commentary — Tara Plues, APRN, MSN

- **Brief Clinical Experiences: 54 year old male with EGFR exon 19. He was started on front-line afatinib 40 mg once daily. No other significant PMHx. Nonsmoker. This patient struggled some with side effects, mostly acne rash and diarrhea. Initially we started clindamycin cream twice daily but had to start him on doxycycline 100 mg twice daily. The doxy aggravated his stomach further in addition to the diarrhea. We were able to decrease the doxy to once daily with topical clinda, moisturizers, face care regimen. For diarrhea he used diphenoxylate/atropine 2 pills 4 times daily as needed in addition to kefir daily (probiotic yogurt beverage). Eventually he was dose reduced to 30 mg once daily and tolerated that better with continued aggressive side effect management.**

Commentary — Tara Plues, APRN, MSN

- **Psychosocial Issues: Anxiety. He was very worried about dose reducing, looked at it very much as a personal failure. He worried the reduced dose wouldn't work and it would be his fault. I also think the side effects were significant but he wouldn't admit that because he was so afraid we would stop his treatment or continue to reduce the dose. This is something we see sometimes… patients try to downplay their symptoms because they fear treatment being stopped.**

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- **EGFR exon 20 insertion mutations**
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- HER2 mutations
- Other targets in NSCLC (MET, ROS1, BRAF, NTRK, NRG1)

Module 4 – Immunotherapy for Localized Disease

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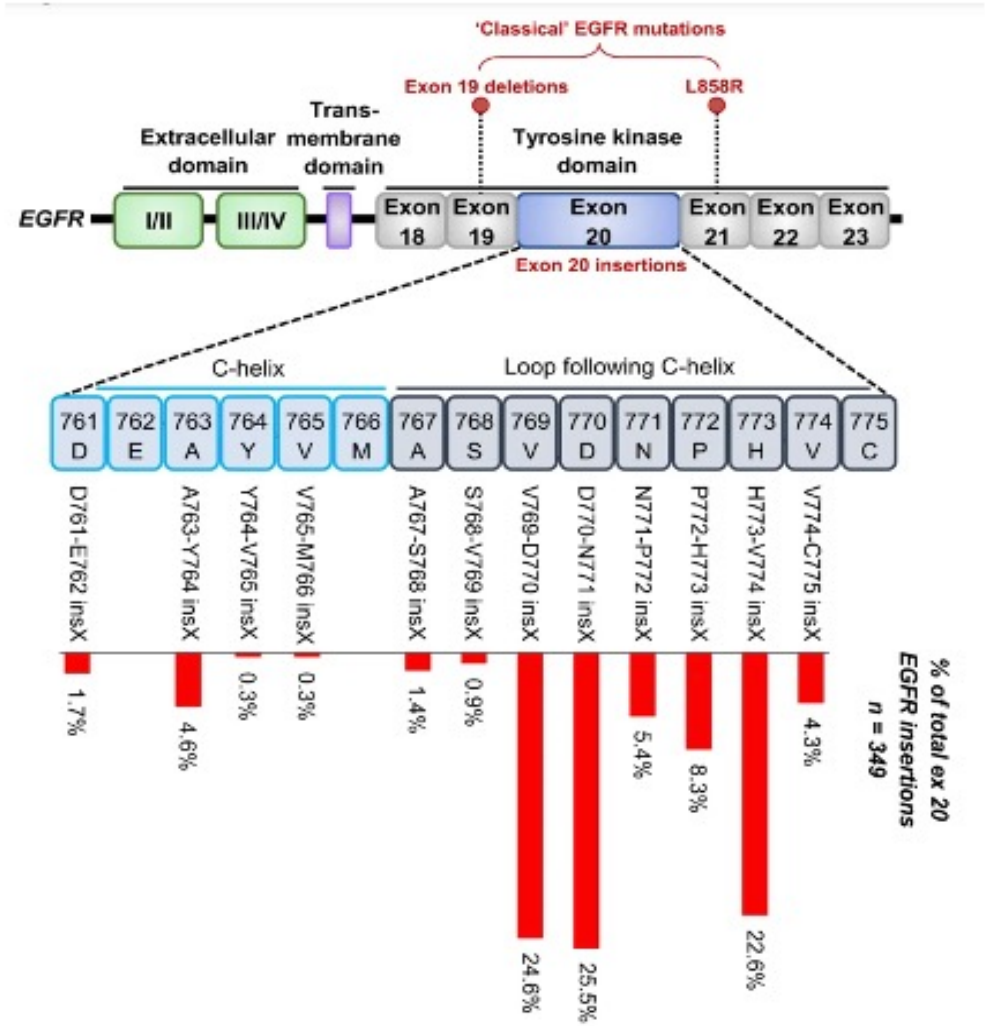
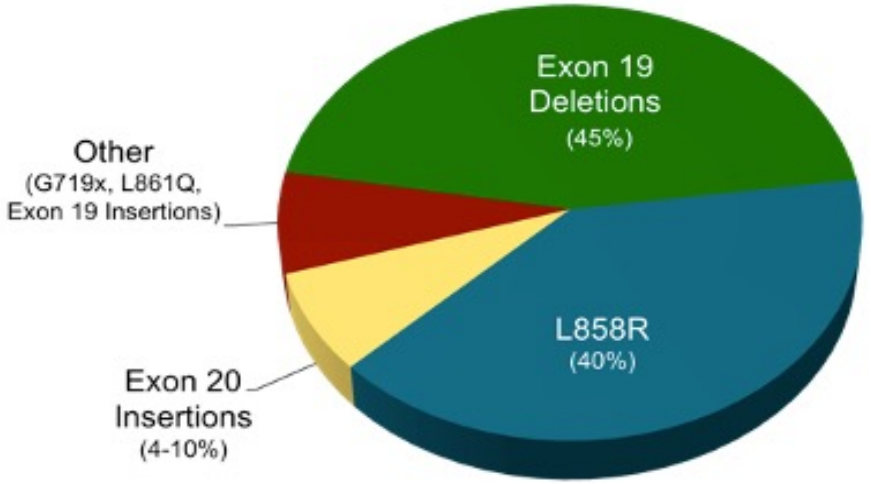
Frequency of EGFR Exon 20 Mutations





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.

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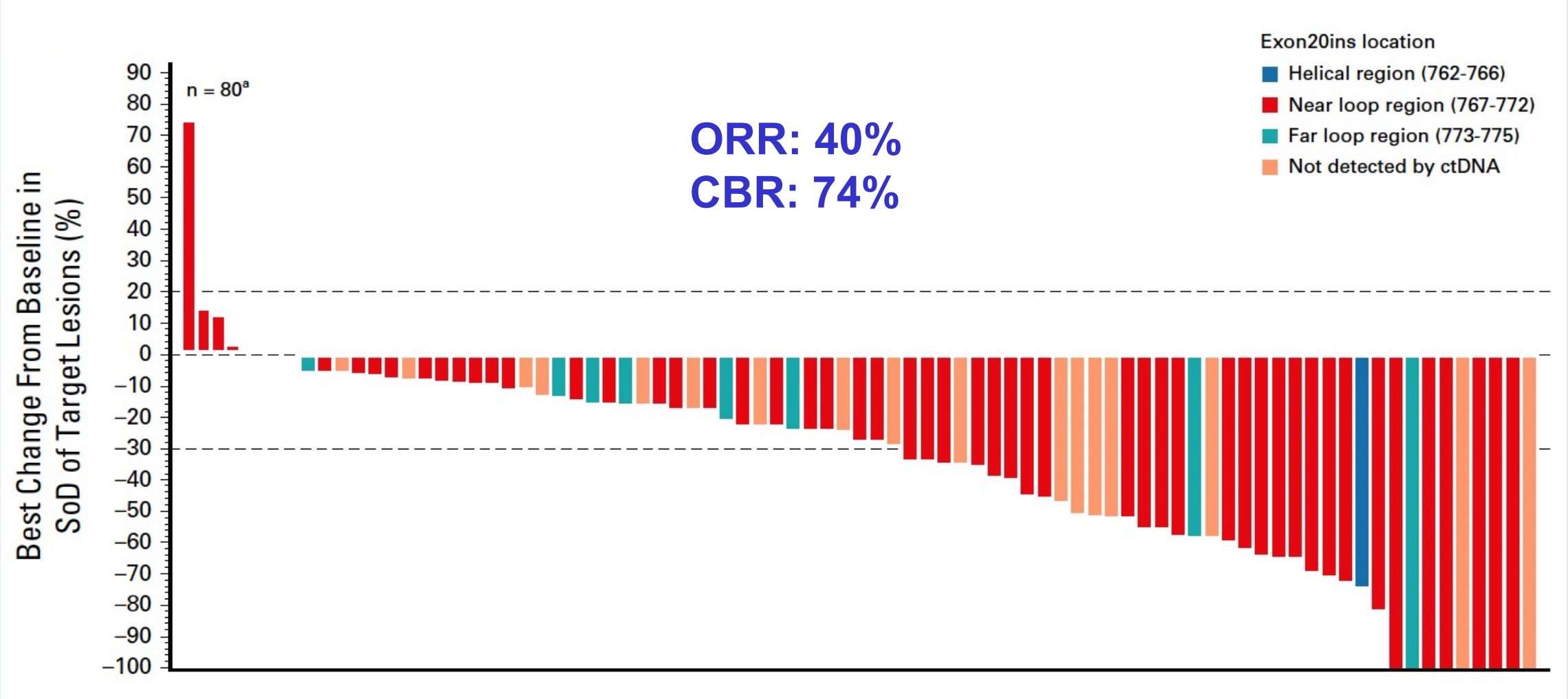
CHRYSALIS: Tumor Reduction and Response with Amivantamab for Advanced NSCLC with an EGFR Exon 20 Insertion Mutation



Park K et al. *J Clin Oncol* 2021;39:3391-402.

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CHRYSALIS: Summary of Adverse Events (AEs) and Most Common AEs

Event	Safety Population (n = 114), No. (%)	Patients Treated at the RP2D (n = 258), No. (%)
Any AE	113 (99)	257 (100)
Grade ≥ 3 AE	40 (35)	101 (39)
Serious AE	34 (30)	79 (31)
AE leading to death	8 (7)	13 (5)
AE leading to discontinuation	11 (10)	17 (7)
AE leading to dose reduction	15 (13)	26 (10)
AE leading to dose interruption[a]	40 (35)	88 (34)

Most Common AEs in the Safety Population

Adverse Events	Any Grade	Grade ≥3
Rash	86%	4%
Infusion-related reactions	66%	3%
Paronychia	45%	1%

Park K et al. *J Clin Oncol* 2021;39:3391-402.

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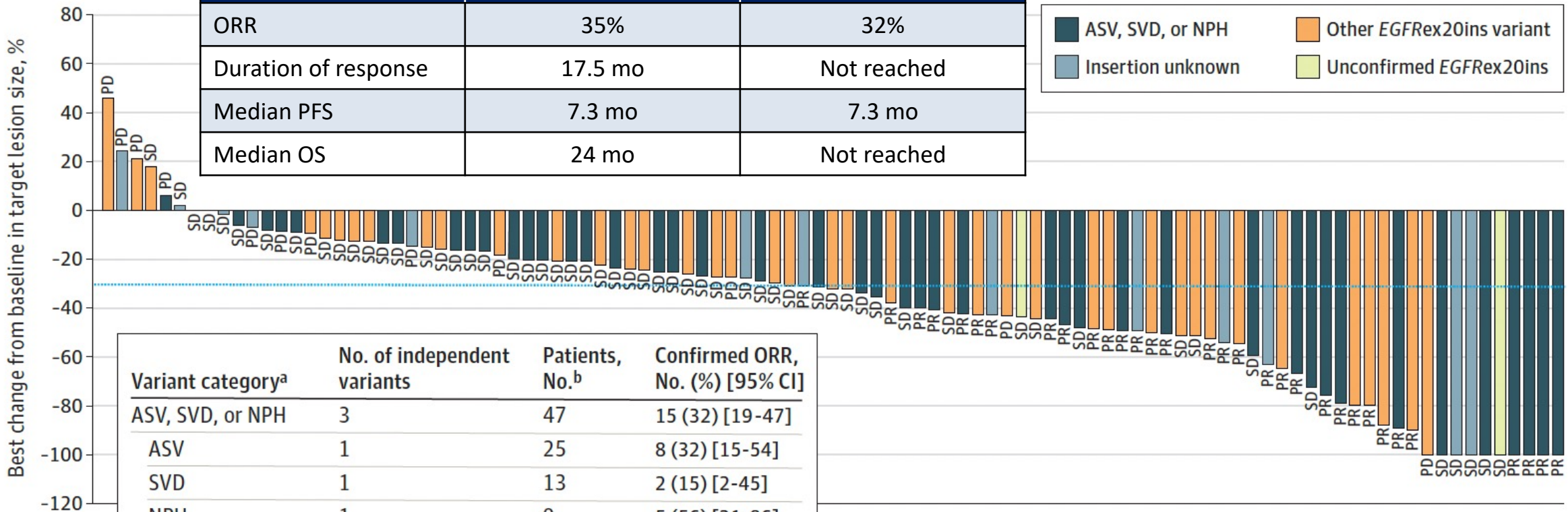
Mobocertinib Activity in Patients with Platinum-Pretreated Metastatic NSCLC with Exon 20 Insertion Mutations (PPP Cohort)

	PPP cohort (n = 114)	EXCLAIM cohort (n = 96)
ORR	35%	32%
Duration of response	17.5 mo	Not reached
Median PFS	7.3 mo	7.3 mo
Median OS	24 mo	Not reached



Variant category[a]	No. of independent variants	Patients, No.[b]	Confirmed ORR, No. (%) [95% CI]
ASV, SVD, or NPH	3	47	15 (32) [19-47]
ASV	1	25	8 (32) [15-54]
SVD	1	13	2 (15) [2-45]
NPH	1	9	5 (56) [21-86]
Other *EGFR*ex20ins	29	48	12 (25) [14-40]
Insertion unknown		16	5 (31) [11-59]

PPP = platinum pretreated patients

Zhou C et al. *JAMA Oncol* 2021 Dec;7(12):e214761.

Summary of Adverse Events (AEs) and Most Common AEs with Mobocertinib

Adverse event	Patients, No. (%)			
	PPP cohort (n = 114)		EXCLAIM cohort (n = 96)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Overview of AEs				
Any	114 (100)	79 (69)	96 (100)	63 (66)
Any treatment-related	113 (99)	54 (47)	95 (99)	40 (42)
Serious	56 (49)	52 (46)	45 (47)	42 (44)
Leading to dose reduction	29 (25)	NA[a]	21 (22)	NA[a]
Leading to treatment discontinuation	19 (17)	NA[a]	10 (10)	NA[a]
Treatment-related AEs of any grade reported in ≥10% or of grade ≥3 reported in ≥3% of patients				
Diarrhea	104 (91)	24 (21)	89 (93)	15 (16)
Rash	51 (45)	0	43 (45)	0
Paronychia	43 (38)	1 (<1)	37 (39)	1 (1)

Zhou C et al. *JAMA Oncol* 2021 Dec;7(12):e214761.

Questions — Kelly EH Goodwin, MSN, RN, ANP-BC

Patients with metastatic NSCLC and an EGFR exon 20 insertion mutation

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are some of the psychosocial issues that arise in this situation?**

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

Patients with metastatic NSCLC and an EGFR exon 20 insertion mutation

- **Similar clinical characteristics to those with common EGFR mutations, but a poorer prognosis**
  - **Younger, female, never-smokers, Asian descent**
- **Symptoms associated with advanced disease include constitutional (fatigue, appetite changes/weight loss), respiratory complaints (dyspnea, cough), pain, neurological complaints**
- **Poorer prognosis, more aggressive disease – may need to palliate symptoms before starting systemic therapy or may need to expedite systemic therapy before molecular diagnostics are available**

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Treatment for metastatic disease is palliative and duration of therapy depends on response and tolerance**
  - **QOL vs quantity – know what matters most to your patient**
  - **Early Palliative Care is important in treating symptoms, managing side effects, empowering patients and families**
- **Not sensitive to EGFR TKIs targeting more common EGFR mutations**
  - **Be hopeful but realistic and honest**
  - **First line chemotherapy (carboplatin/pemetrexed) side effects include fatigue, appetite/taste changes, bone marrow changes including immunosuppression, GI side effects, renal or hepatic dysfunction, electrolyte imbalances, neurotoxicity (neuropathy, tinnitus, hearing changes), rash, fluid retention, allergic reactions**
  - **Avoid immunotherapy given poor response, increased risk of toxicity with subsequent TKI**

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TO PRACTICE

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Mobocertinib – TKI approved in 2nd line setting and beyond**
  - **Oral therapy is convenient but not without significant toxicities**
    - **Traditional EGFR TKI class effects – GI toxicity, skin/nail toxicity, transaminitis, pneumonitis**
      - **QTc prolongation and torsades de pointes**
  - **Compliance with oral therapy, reliability with reporting and aggressively treating side effects**
    - **Set expectations for dose interruptions and dose modifications, though recognize could impact response**
- **Amivantamab – biphasic EGFR and MET receptor antibody in 2nd line setting and beyond**
  - **IV treatment may be less convenient but is frequently preferred**
  - **Set appropriate expectations about risk of infusion reactions and side effects**
    - **Premedicate with glucocorticoids, antihistamine, antipyretic**
    - **Week 1 dosed on days 1, 2 then weekly through week 4 then q2 weeks**
- **Patients may experience traditional EGFR effects (skin) and MET effects (edema)**

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Stigma associated with lung cancer diagnosis**
  - **Treatment side effects can reveal diagnosis patient is trying to conceal or minimize**
- **Younger patients balancing families, work**
  - **Palliative Care, Psych-Onc, Parenting At a Challenging Time (PACT)**
- **Prognosis and treatment options and responses very different from more common EGFR mutation patients**
  - **Find appropriate supports/resources online, managing expectations**
- **Treatment decisions (mobocertinib vs amivantamab vs clinical trial enrollment) can depend on patient factors – transportation, support, insurance coverage, reliability**

RTP
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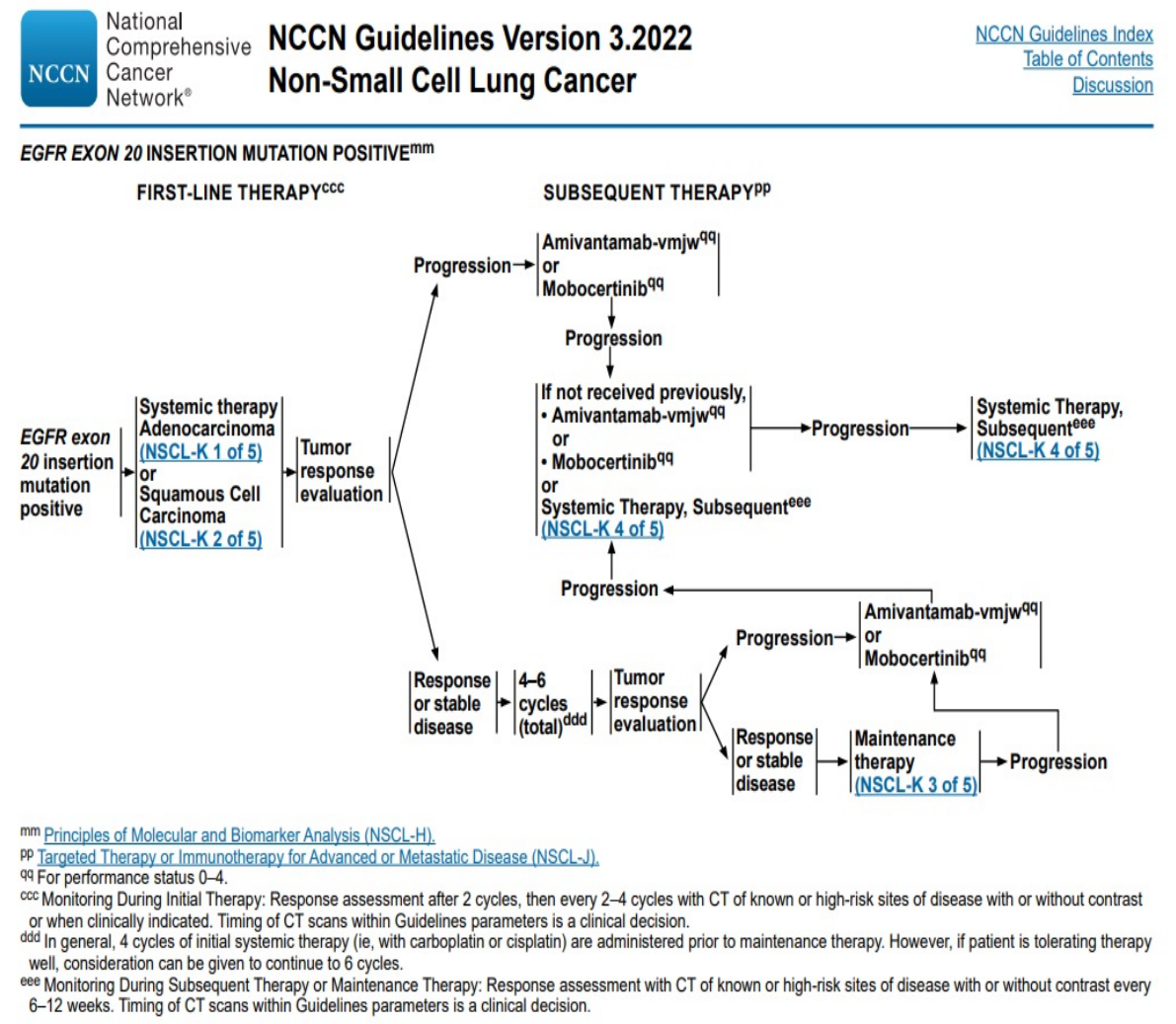
TO PRACTICE

Questions — Anne S Tsao, MD, MBA

Patients with metastatic NSCLC and an EGFR exon 20 insertion mutation

- **What therapies are used to treat metastatic NSCLC with an EGFR exon 20 insertion mutation, and how is treatment selected?**
- **Please cite brief instructive examples of actual clinical experiences with patients in your practice.**

EGFR Exon 20 New Agents



	Mobocertinib	Amivantamab
FDA approval date	Sept 15, 2021	May 21, 2021
Type of agent	TKI	Bispecific antibody to EGFR and MET receptor
Delivery	Oral	IV
Schedule	160 mg Daily +/- food	IV weekly (QW) for 4 weeks, with the initial dose as a split infusion in week 1 on day 1 and day 2, then every 2 weeks (Q2W) starting at Week 5
Premeds	No	Yes (diphenhydramine, acetaminophen, dexamethasone week 1 d1-2 then prn)
Most common side effects	Diarrhea, rash, nausea, stomatitis, vomiting, decreased appetite, paronychia, fatigue, dry skin, and musculoskeletal pain	Rash, paronychia, infusion-related reactions, muscle and joint pain, shortness of breath, nausea, fatigue, peripheral or general edema, oral sores, cough, constipation, vomiting
Toxicities to note	QTc prolongation, decreased EF, stomatitis, ILD/pneumonitis, diarrhea, increased LFTs	Infusion related reaction, dermatologic toxicity, ocular toxicity, ILD/pneumonitis

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **42yo F, never smoker, no PMH presents to PCP with cough, sensation of lump in throat in 2/2014. CT Chest with 3.1cm RUL and bilateral hilar and precarinal, subcarinal, prevascular LAD. Stage IIIA → downstaged to IIA with mediastinoscopy revealing sarcoid granulomatous disease and multiple nodes. Path reveals EGFR exon 20 insertion mutation**
  - **Neoadjuvant cis/pem x 2 with concurrent XRT → RUL lobectomy → cis/pem x 2**
  - **Recurrence in R post-auricular LN after 3 years; resected; NED since**
- **62yo M, never smoker, no PMH presents to ED for chest pain and dyspnea following chiropractic manipulation for chronic back pain and found to have RLL mass, extensive adenopathy, vertebral mets, ? punctate enhancement/met on MRI Brain. Workup ultimately reveals metastatic NSCLC with exon 20 insertion mutation**

RTP RESEARCH TO PRACTICE

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Palliative RT to L5 lytic lesion**
- **First line therapy with TAK788 (mobocertinib) on clinical trial**
  - **Required dose modification for diarrhea, taste changes/weight loss**
  - **CNS progression after 8 months – completed HA-WBRT, continued TAK788 post-progression**
    - **5 months later developed vision changes, dizziness, neck pain/stiffness, back pain and found to have diffuse leptomeningeal disease.**
      - **Carbo/pem x 2 with progressive symptoms and functional decline**

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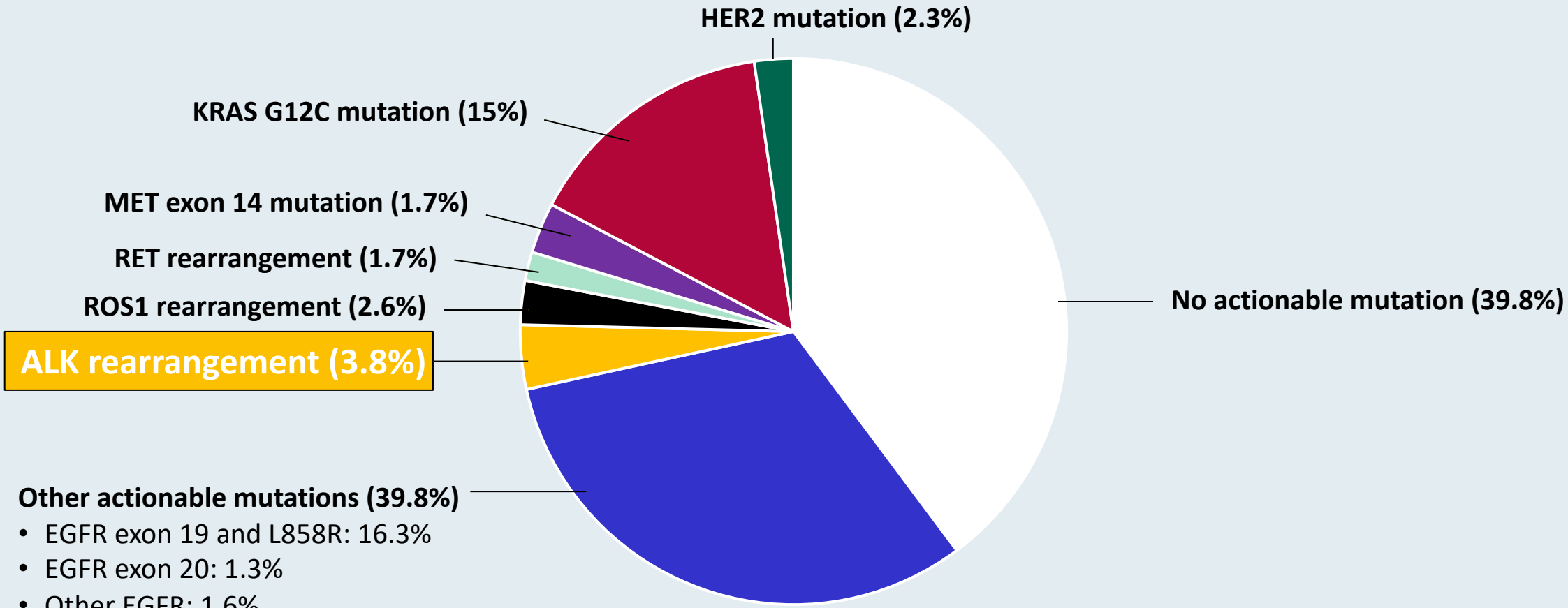
Module 4 – Immunotherapy for Localized Disease

Module 5 – Immunotherapy for Metastatic Disease

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung

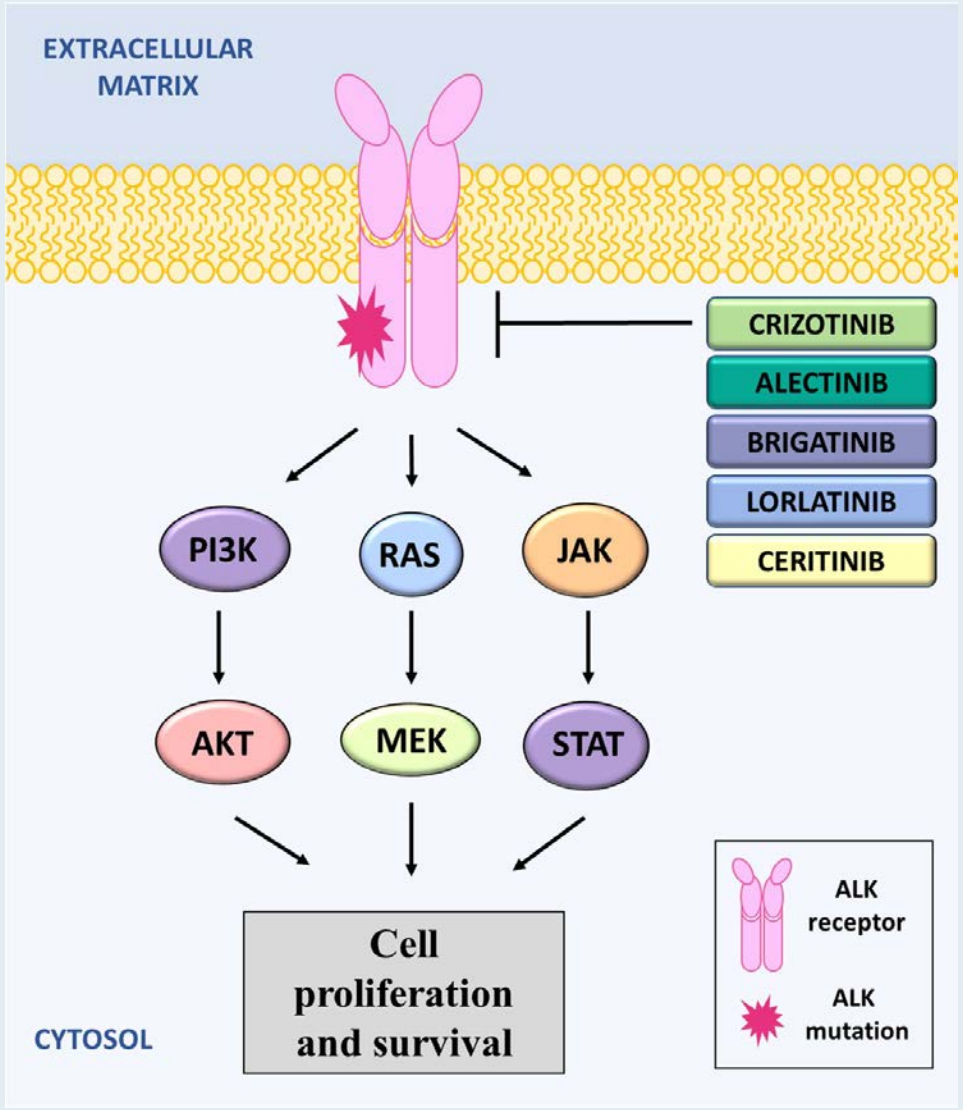


- EGFR exon 19 and L858R: 16.3%
- EGFR exon 20: 1.3%
- Other EGFR: 1.6%
- Other KRAS: 10.3%
- BRAF V600E: 2.1%
- NTRK rearrangement: 0.23%

Derived from Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

RTP RESEARCH TO PRACTICE

Mechanism of Action of ALK Inhibitors



3-13% of NSCLCs

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

Questions — Tara Plues, APRN, MSN

Patients with a prolonged response to targeted treatment

- **What are some of the psychosocial issues that arise in this situation?**

Commentary — Tara Plues, APRN, MSN

Patients with a prolonged response to targeted treatment

- 48 year old female initially stage IIIA NSCLC diagnosed in 2007. (Social history: married with 2 grown children, now with one grandchild, works full time in the hotel industry. Family is very supportive)
- Initially treated with neoadjuvant paclitaxel/carboplatin/XRT, right pneumonectomy, adjuvant chemo (same) followed by erlotinib on clinical trial
- Progressed on trial (on erlotinib) in 2008
- At that time (December 2008) was started on carboplatin/pemetrexed/bevacizumab
  - Carboplatin was stopped due to a carbo reaction
  - Bevacizumab was stopped after a few cycles due to pt preference
  - Pemetrexed was continued through June 2010. NED. Decision was made mutually to stop treatment

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Commentary — Tara Plues, APRN, MSN

- **In 2017 she developed an isolated spine metastasis, treated with SRS. Genomic testing revealed ALK rearrangement. Started on alectinib at that time.**
- **She is NED currently and continues on alectinib 600 mg twice daily.**

Psychosocial Issues:

- **Due to the chronicity of the disease and tolerability of medications used thus far there are high expectations for quality of life and side effect management.**
  - **Example: she has some leg swelling, was worse with first starting alectinib. This was very bothersome for her.**
  - **Maintaining appearances at work and with friends is very important to her. Dealing with dyspnea from pneumonectomy, leg swelling from alectinib and weight gain from being less active have been bothersome to her.**
- **She has a significant amount of anxiety knowing medications will stop working at some point and that her cancer is not curable.**

RTP RESEARCH TO PRACTICE

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Module 4 – Immunotherapy for Localized Disease

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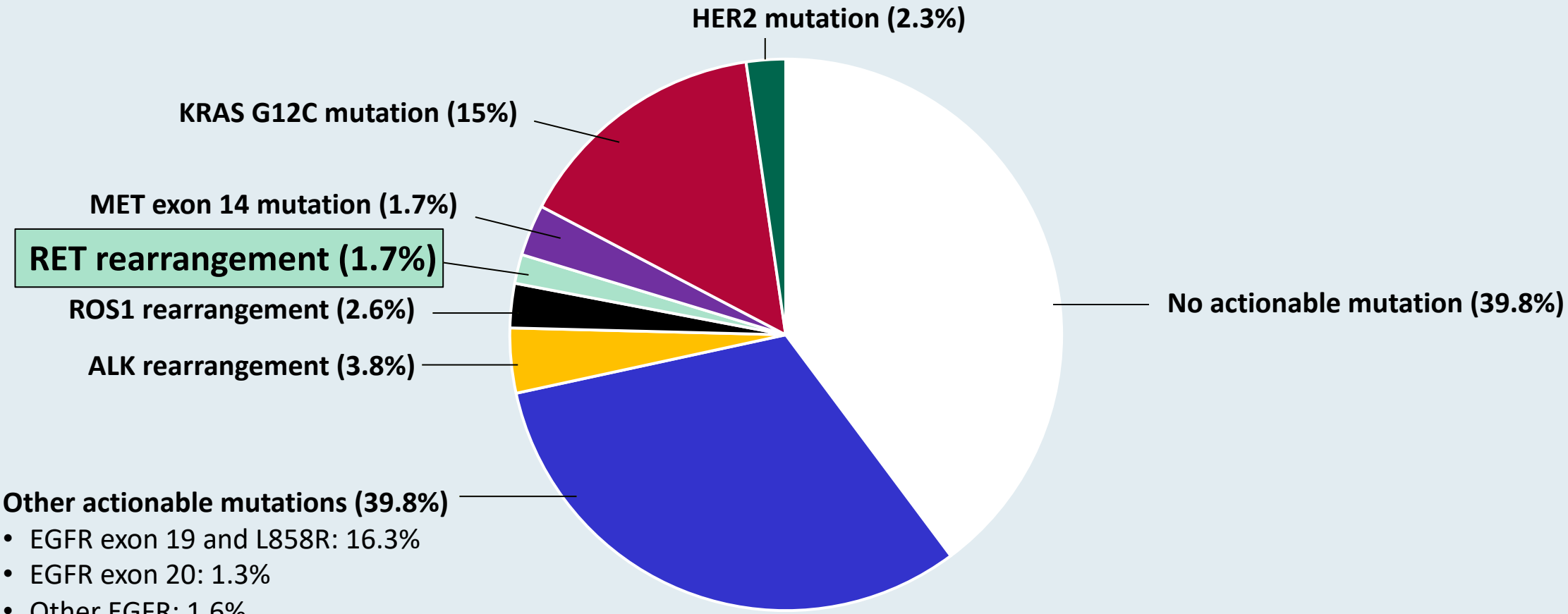
SELF-ASSESSMENT QUIZ

Response rates higher than 50% have been reported with targeted agents for patients with a…

1. BRAF mutation
2. RET rearrangement
3. NTRK fusion
4. MET exon 14 alteration
5. All of the above
6. Only 1 and 2
7. I don’t know

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung

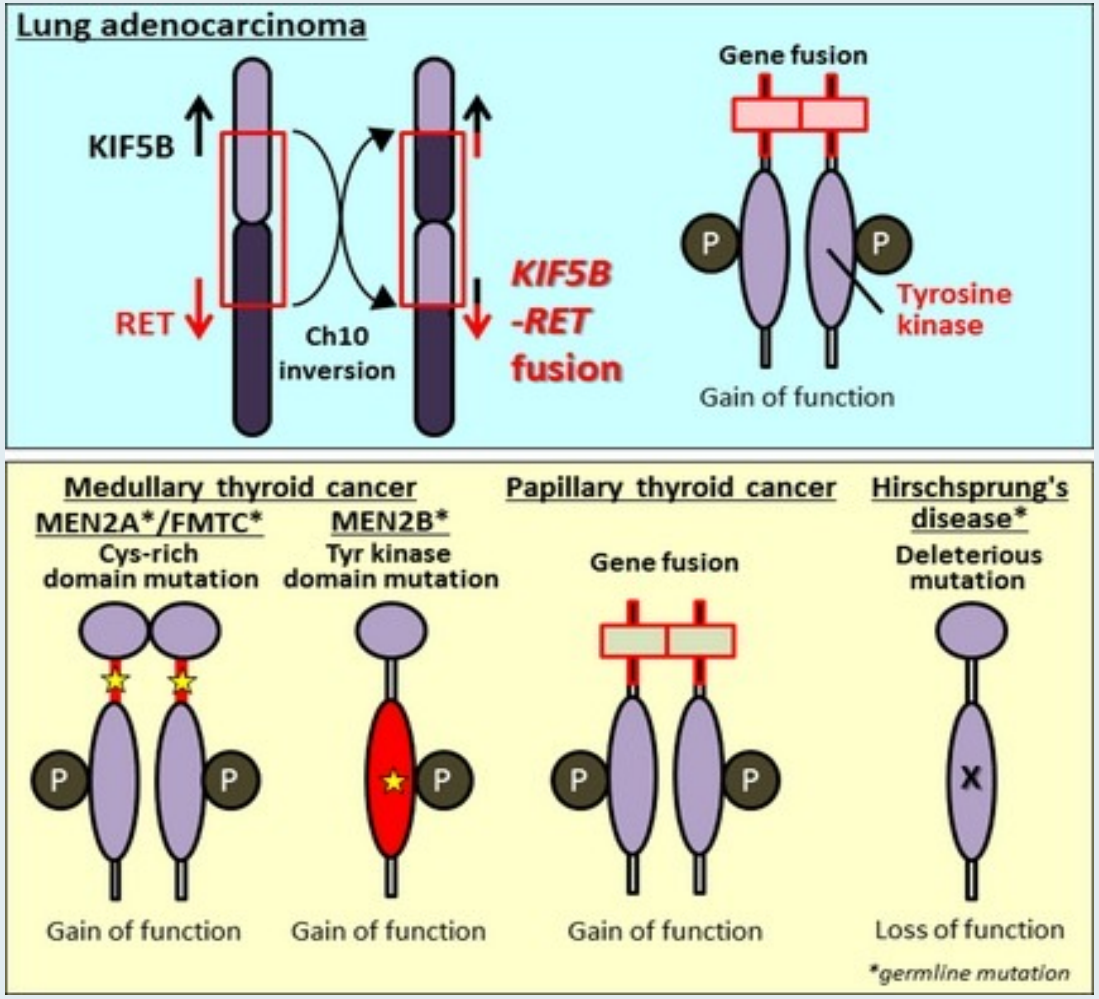


- EGFR exon 19 and L858R: 16.3%
- EGFR exon 20: 1.3%
- Other EGFR: 1.6%
- Other KRAS: 10.3%
- BRAF V600E: 2.1%
- NTRK rearrangement: 0.23%

Derived from Tan AC et al. *J Clin Oncol* 2022;40:611-625.

RTP RESEARCH TO PRACTICE

RET Fusions in NSCLC



- Intact tyrosine kinase domain fused to an upstream gene partner
  - most common: *KIF5B*
  - others: *CCDC6, NCOA4, TRIM33, KIAA1468*
- Ligand-independent dimerization and downstream growth pathway activation
- Oncogenic *in vitro* and *in vivo*
- 1-2% NSCLC; younger; never/light smokers; adenocarcinoma/poorly differentiated

Drilon AD, Cancer Discov 2013;3:630-5, Kohno T, Nat Med 2012;18:375-7, Saito M, Carcinogenesis 2014;35:2452-6;Suehara Y, Nat Med 2012;18;6599-608, Lipson D, Nat Med 2012;18:382-40, Takeuchi K, Nat Med 2012;18:378-81

RTP RESEARCH TO PRACTICE

Selpercatinib and Pralsetinib for Advanced NSCLC with RET Fusion

	Selpercatinib[1]	Pralsetinib[2]
Pivotal study	LIBRETTO-001 Phase I/II (N = 105)	ARROW Phase I/II (N = 233)
FDA approval	May 8, 2020	September 4, 2020
ORR	64%	61%
Median duration of response	17.5 months	Not reached
Common Grade ≥3 adverse events	Hypertension (14%) Increased ALT (12%) and AST (10%) levels Hyponatremia (6%) Lymphopenia (6%)	Neutropenia (18%) Hypertension (11%) Anemia (10%) Decreased WBC (6%)

[1] Drilon A et al. *N Engl J Med* 2020;383:813-24. [2] Gainor JF et al. *Lancet Oncol* 2021;22:959-69.

RTP RESEARCH TO PRACTICE

Questions — Edward B Garon, MD, MS

Patients with metastatic NSCLC and a RET fusion

- **What therapies are used to treat metastatic NSCLC with a RET fusion, and how is treatment selected?**

Commentary – Edward B Garon, MD, MS

Patients with metastatic NSCLC and a RET fusion

- **The option should clearly be selpercatinib or pralsetinib**
- **I think that practitioners choose based on familiarity**
- **We participated in selpercatinib trials, so I have used that**
- **Two examples off trial indicate the spectrum of results:**
  - **Patient 1 has been on drug since shortly after approval, leading a normal life**
  - **Patient 2 had significant LFT abnormalities requiring drug discontinuation**

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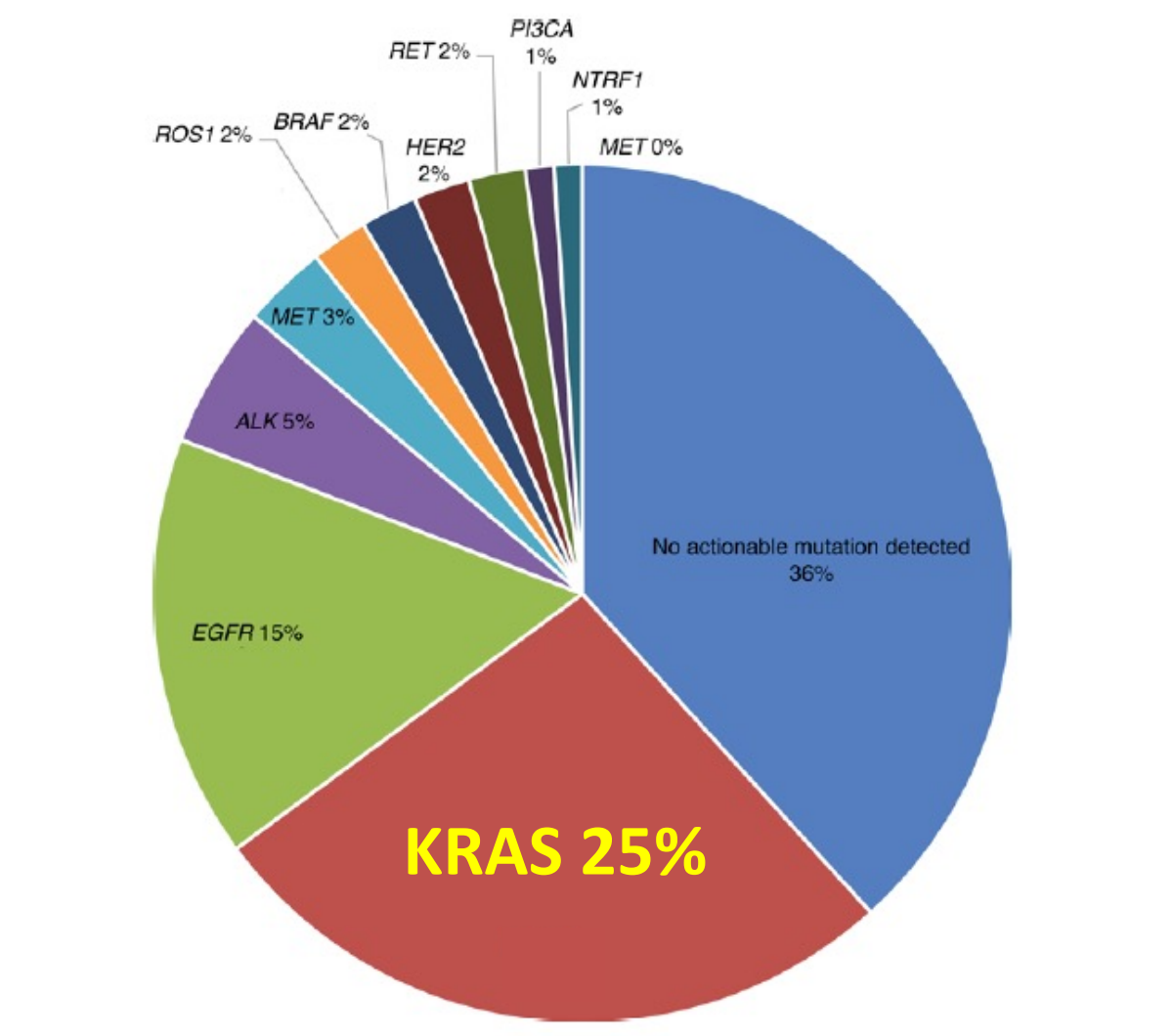
RTP RESEARCH TO PRACTICE

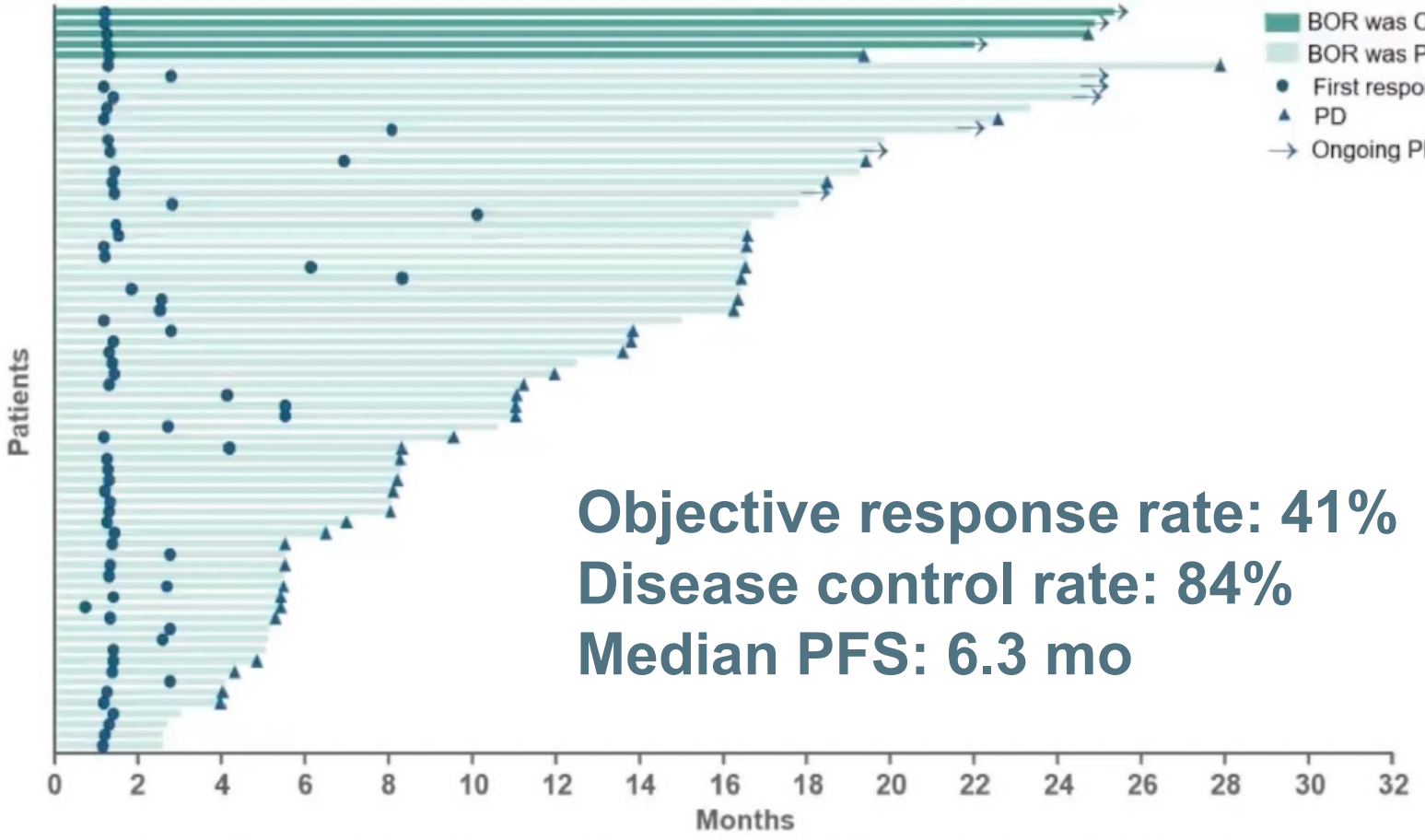
Frequency of Targetable Oncogenic-Driver Molecular Alterations in Adenocarcinoma of the Lung



Pakkala S, Ramalingam SS. *JCI Insight* 2018;3(15):e120858.

CodeBreaK 100: Long-Term Outcomes with Sotorasib for Pre-Treated Metastatic NSCLC with KRAS G12C Mutation

— *Durability of Response*



Objective response rate: 41%
Disease control rate: 84%
Median PFS: 6.3 mo

Median time to response: 6 weeks

- 70% of patients had a response at their first scan

Median duration of response: 12.3 months (95% CI: 7.1, 15.0)

50.6% (95% CI: 37.4, 62.4) **of responders remained in response for 12+ months**

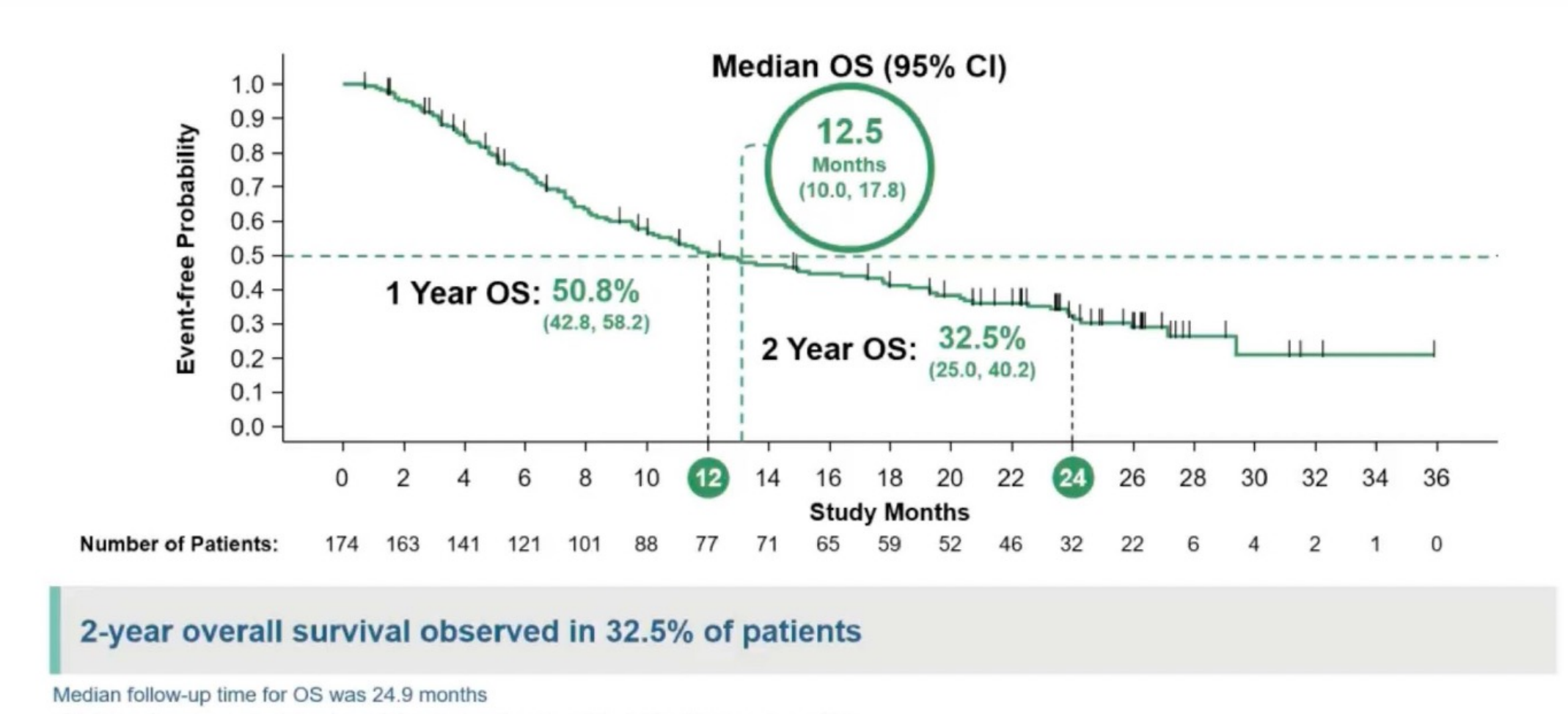
BOR, best overall response; CR, complete response; PD, progressive disease; PFS, progression-free survival; PR, partial response.

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Long-Term Outcomes with Sotorasib for Pre-Treated Metastatic NSCLC with KRAS G12C Mutation

— *Overall Survival*

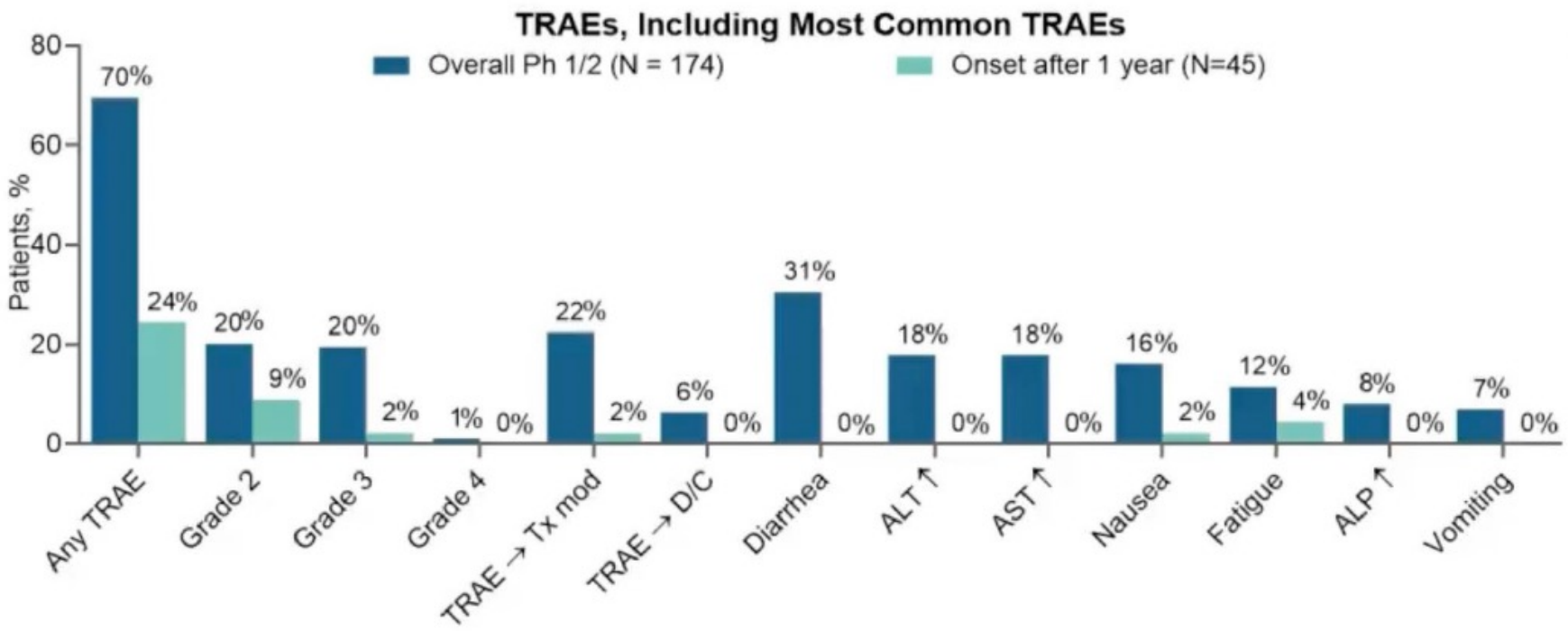


Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Long-Term Outcomes with Sotorasib for Pre-Treated Metastatic NSCLC with KRAS G12C Mutation

— *Treatment-Related Adverse Events (TRAEs)*



Grade 3 or 4 TRAEs occurred in 21% of patients

- One patient with new onset Grade 3 TRAE after 1 year (hemolytic anemia)

No fatal TRAEs occurred

- No TRAE leading to discontinuation after 1 year

Well-tolerated in the long-term: late-onset TRAEs were mild and manageable

Dy GK et al. AACR 2022;Abstract CT008.

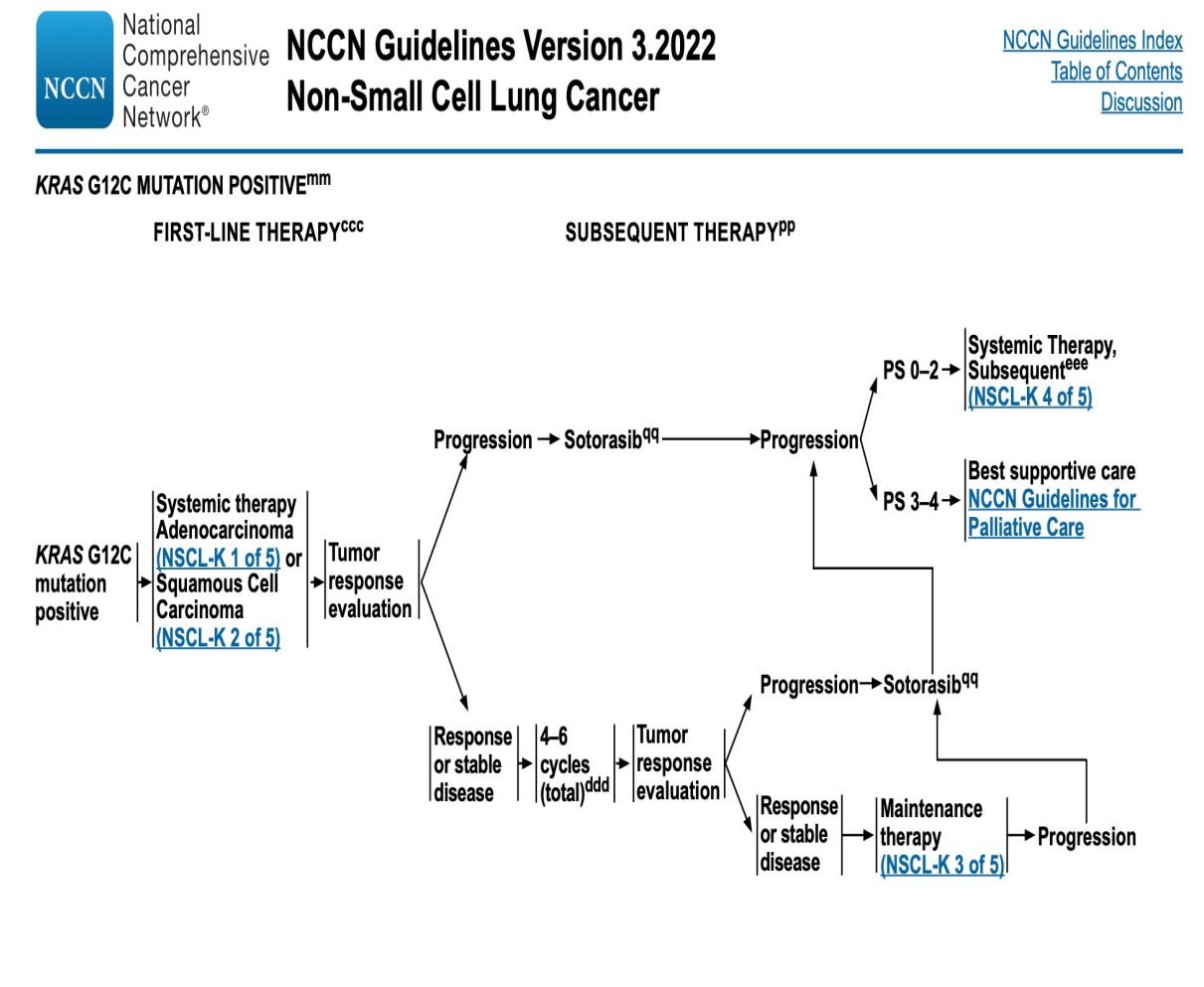
RTP RESEARCH TO PRACTICE

Questions — Anne S Tsao, MD, MBA

Patients with metastatic NSCLC and a KRAS G12C mutation

- **What therapies are used to treat metastatic NSCLC with a KRAS G12C mutation, and how is treatment selected?**
- **Please cite brief instructive examples of actual clinical experiences with patients in your practice.**

KRAS G12C



	Sotorasib (AMG-510)
FDA approval date	May 28, 2021
Type of agent	TKI
Delivery	Oral
Schedule	960 mg Daily +/- food
Premeds	No
Most common side effects	diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity, and cough, decreased lymphocytes, decreased Hgb, increased LFTs, decreased calcium, increased alk phos, proteinuria, and decreased sodium
Other KRAS G12C agents	MRTX849, ARS-1620, ARS-3248, JNJ-74699157, LY3499446

RTP RESEARCH TO PRACTICE

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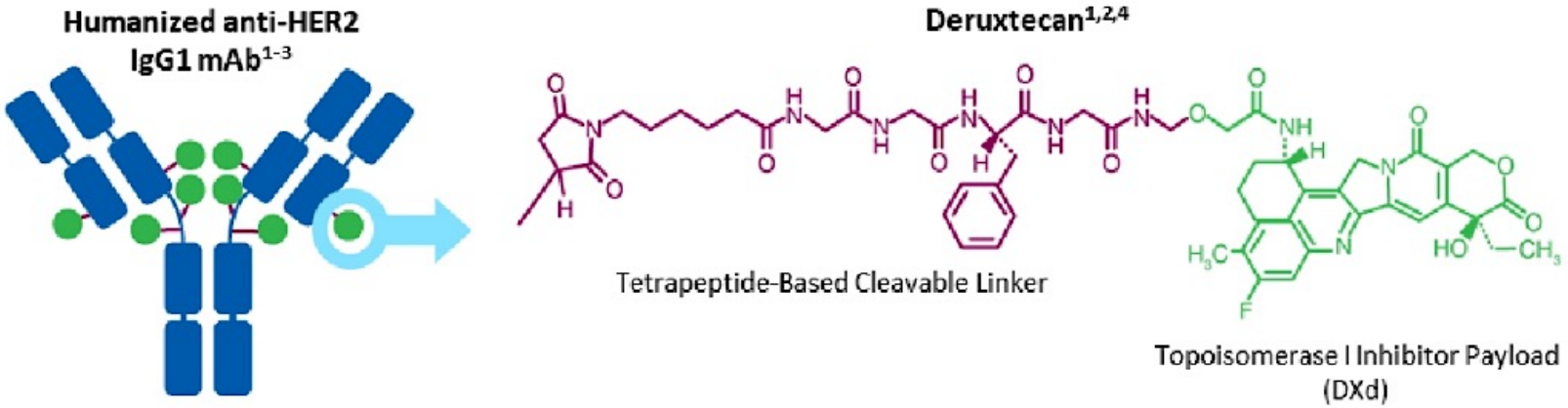
Module 4 – Immunotherapy for Localized Disease

Module 5 – Immunotherapy for Metastatic Disease

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

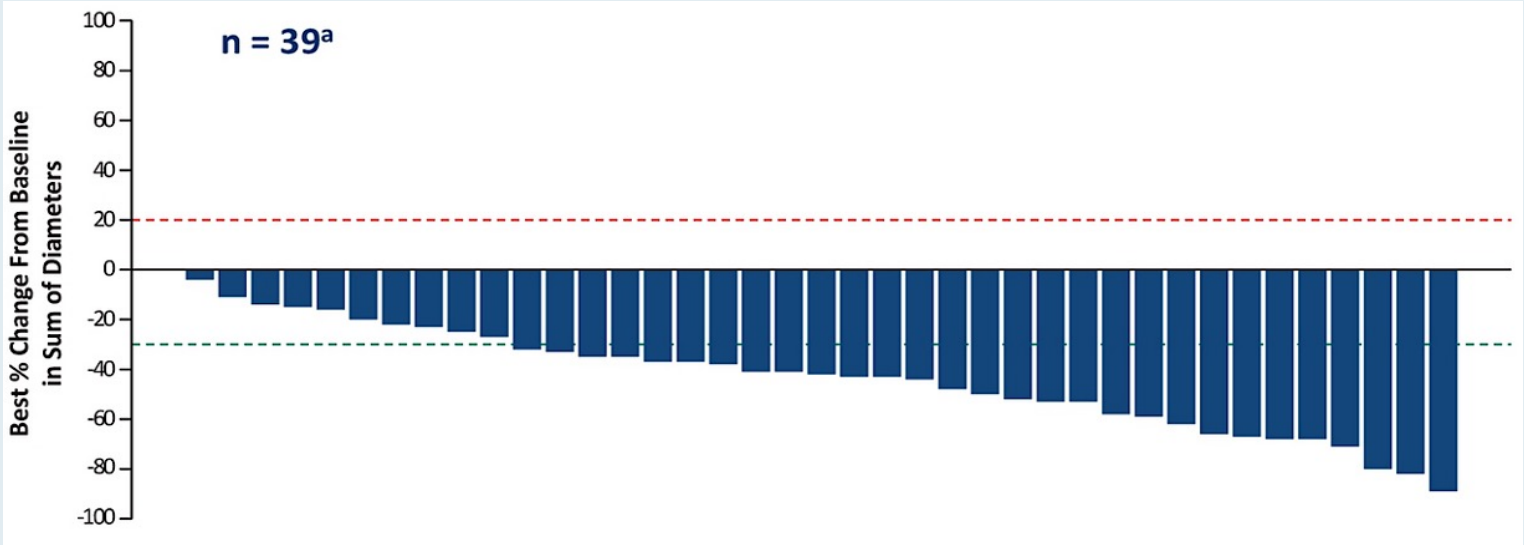


Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug to antibody ratio ≈ 8
Payload with short systemic half-life
Stable linker-payload
Tumor-selective cleavable linker
Membrane-permeable payload

Smit EF et al. ASCO 2020;Abstract 9504.

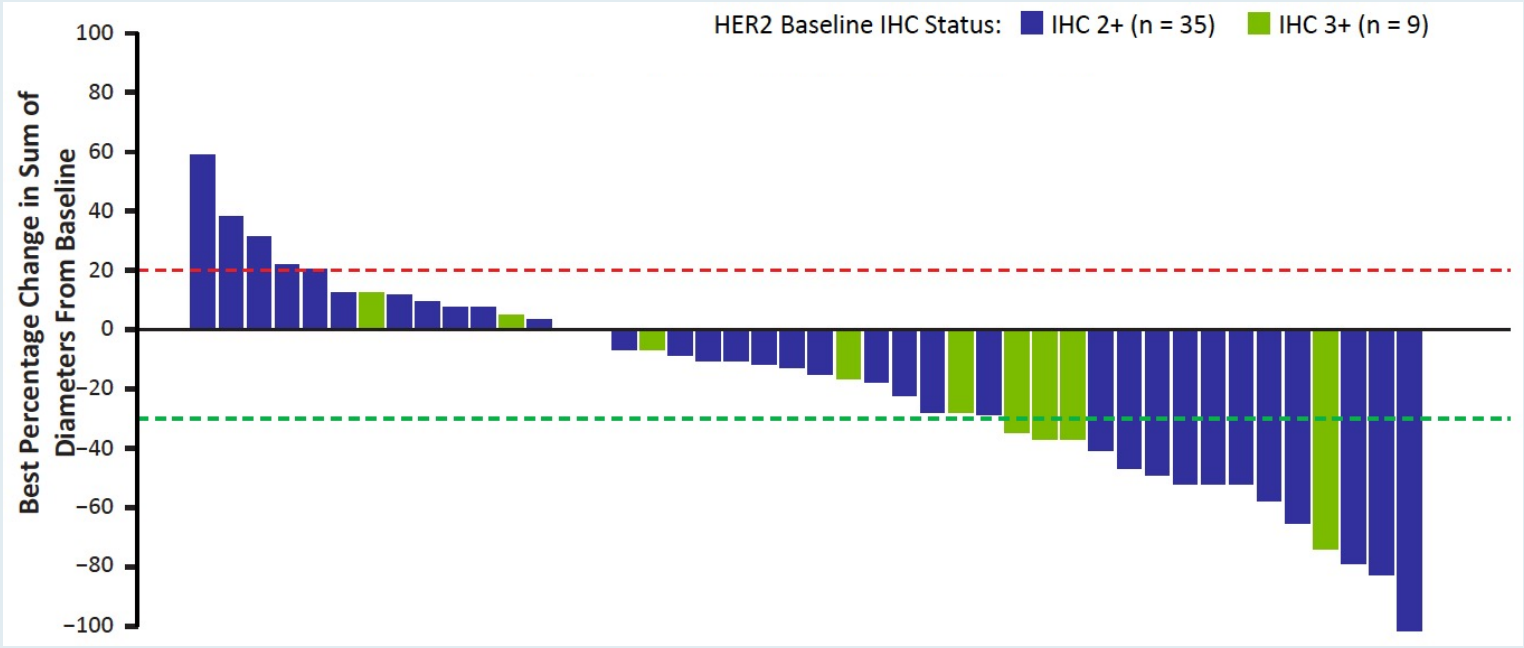
DESTINY-Lung01: Best Percentage Change in Tumor Size with T-DXd in NSCLC with HER2 Mutation versus Overexpression

Mutation



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

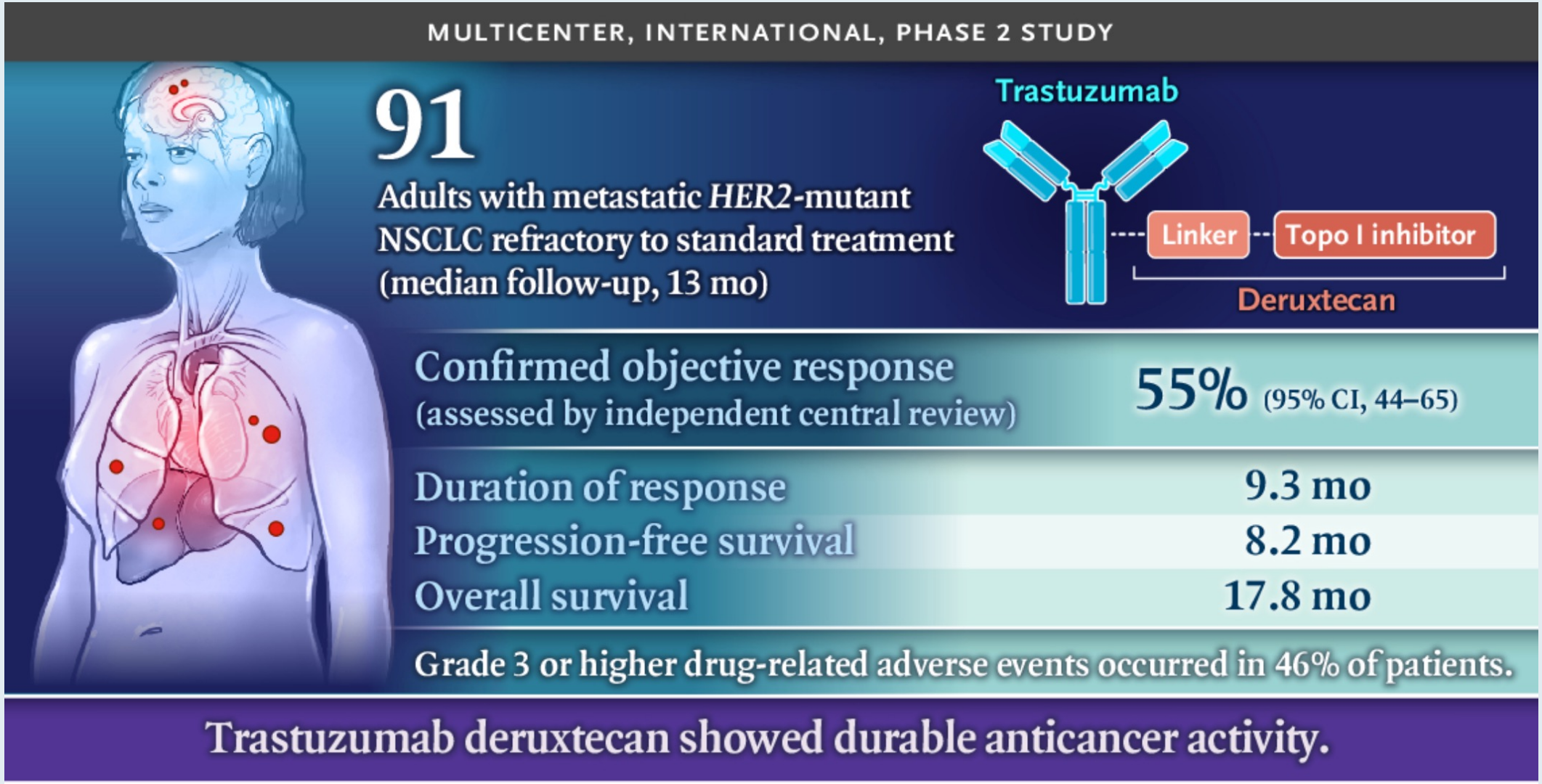
Overexpression



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.

DESTINY-Lung01: Activity of Trastuzumab Deruxtecan in Patients with Advanced NSCLC with HER2 Mutations



Li BT et al. *N Engl J Med* 2022;386(3):241-51.

DESTINY-Lung01: Summary of Adverse Events and AEs of Clinical Interest

Event	N = 91
Discontinuation due to AEs	25%
Dose reduction due to AEs	34%
Dose interruption due to AEs	32%
Drug-related interstitial lung disease (ILD)	26% (N = 24)
Grade 1	3 pts
Grade 2	15 pts
Grade 3	4 pts
Grade 5	2 pts
Median time to onset of ILD	141 days
Median duration of ILD	43 days

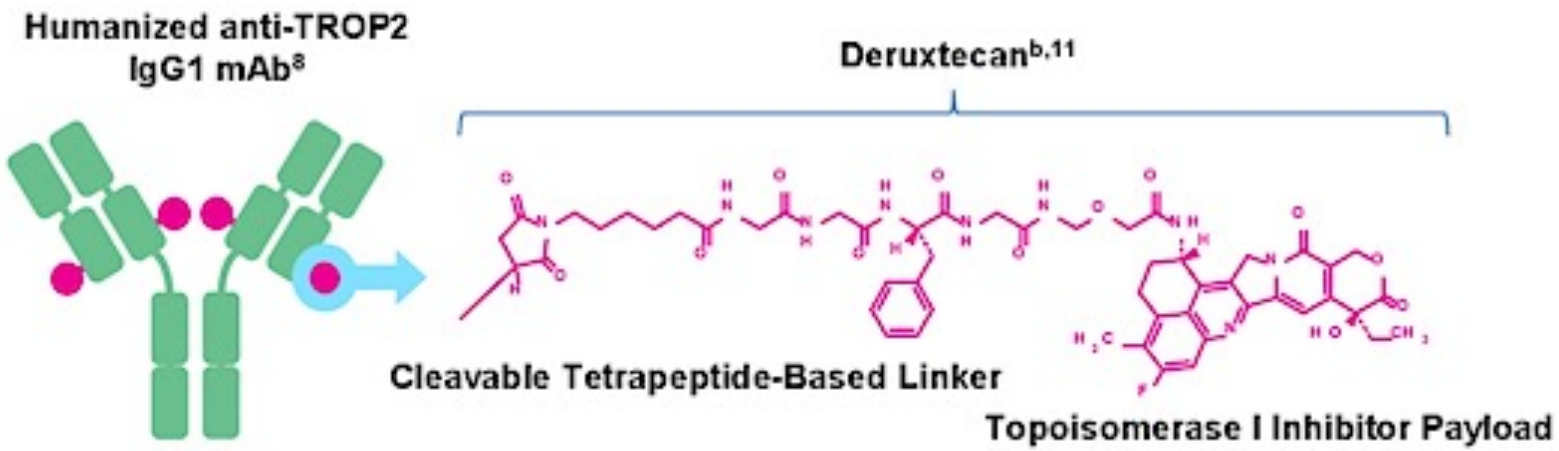
Li BT et al. *N Engl J Med* 2022;386(3):241-51.

DESTINY-Lung01: Common Adverse Events (N = 91)

Event	Any grade	Grade ≥3
Nausea	73%	9%
Fatigue	53%	7%
Alopecia	46%	0
Vomiting	40%	3%
Neutropenia	35%	18%
Anemia	33%	10%
Diarrhea	32%	3%
Decreased appetite	30%	0
Leukopenia	23%	4%
Constipation	22%	0

Li BT et al. *N Engl J Med* 2022;386(3):241-51.

Datopotamab Deruxtecan: TROP2-Targeted Antibody-Drug Conjugate



Designed With 7 Key Attributes:

- Payload mechanism of action: topoisomerase I inhibitor [a,6]
- High potency of payload [a,7]
- Optimized DAR ≈4 [a,c,6]
- Payload with short systemic half-life [a,c,7]
- Stable linker-payload [a,7]
- Tumor-selective cleavable linker [a,7]
- Bystander antitumor effect [a,7,12]

mAB, monoclonal antibody; TROP2, trophoblast cell-surface antigen 2.
[a] The clinical relevance of these features is under investigation.
[b] Actual drug positions may vary.
[c] Based on animal data.

Meric-Bernstam F et al. ASCO 2021;Abstract 9058.

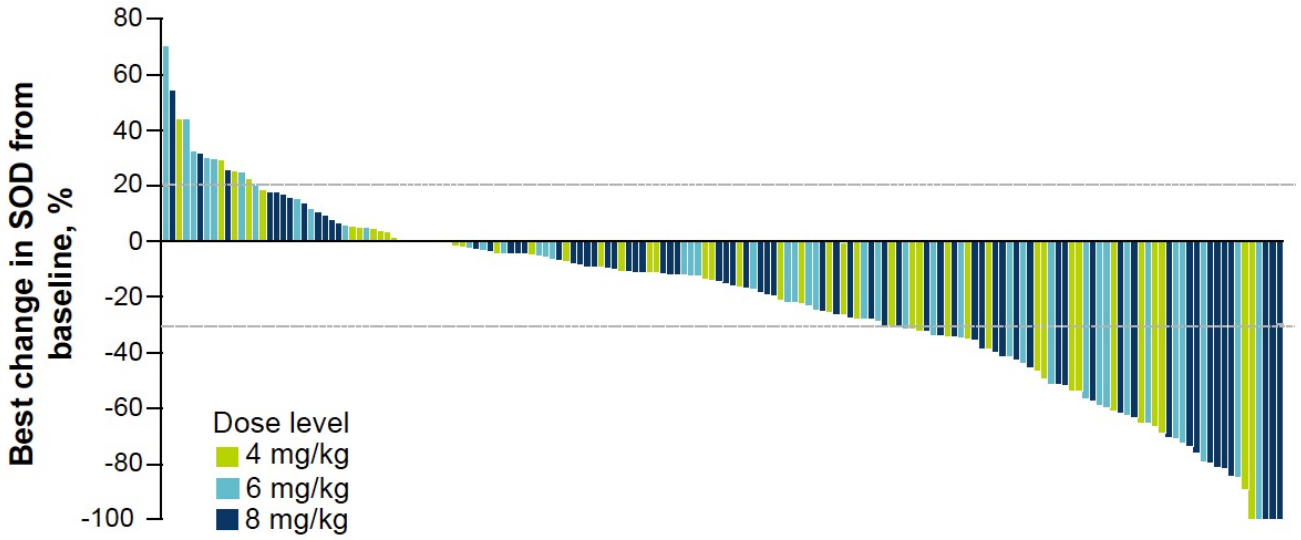
RTP RESEARCH TO PRACTICE

TROPION-PanTumor01: Updated Results from the NSCLC Cohort in the Phase I Study of Datopotamab Deruxtecan in Solid Tumors

Best Overall Response (BICR)

Patients[a]	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
ORR, n (%)[b]	12 (24)	14 (28)	19 (24)
CR, n (%)	0	0	1 (1)
PR, n (%)[b]	12 (24)	14 (28)	18 (23)
SD, n (%)	25 (50)	20 (40)	42 (53)
Non-CR/PD, n (%)	1 (2)	2 (4)	2 (3)
PD, n (%)	7 (14)	10 (20)	8 (10)
NE, n (%)	5 (10)	5 (10)	9 (11)
DOR, median (95% CI), mo	NE (2.8-NE)	10.5 (5.6-NE)	9.4 (5.8-NE)

Best Change in Sum of Diameters (per BICR)



Garon EB et al. World Conference on Lung Cancer 2021;Abstract MA03.02.

RTP RESEARCH TO PRACTICE

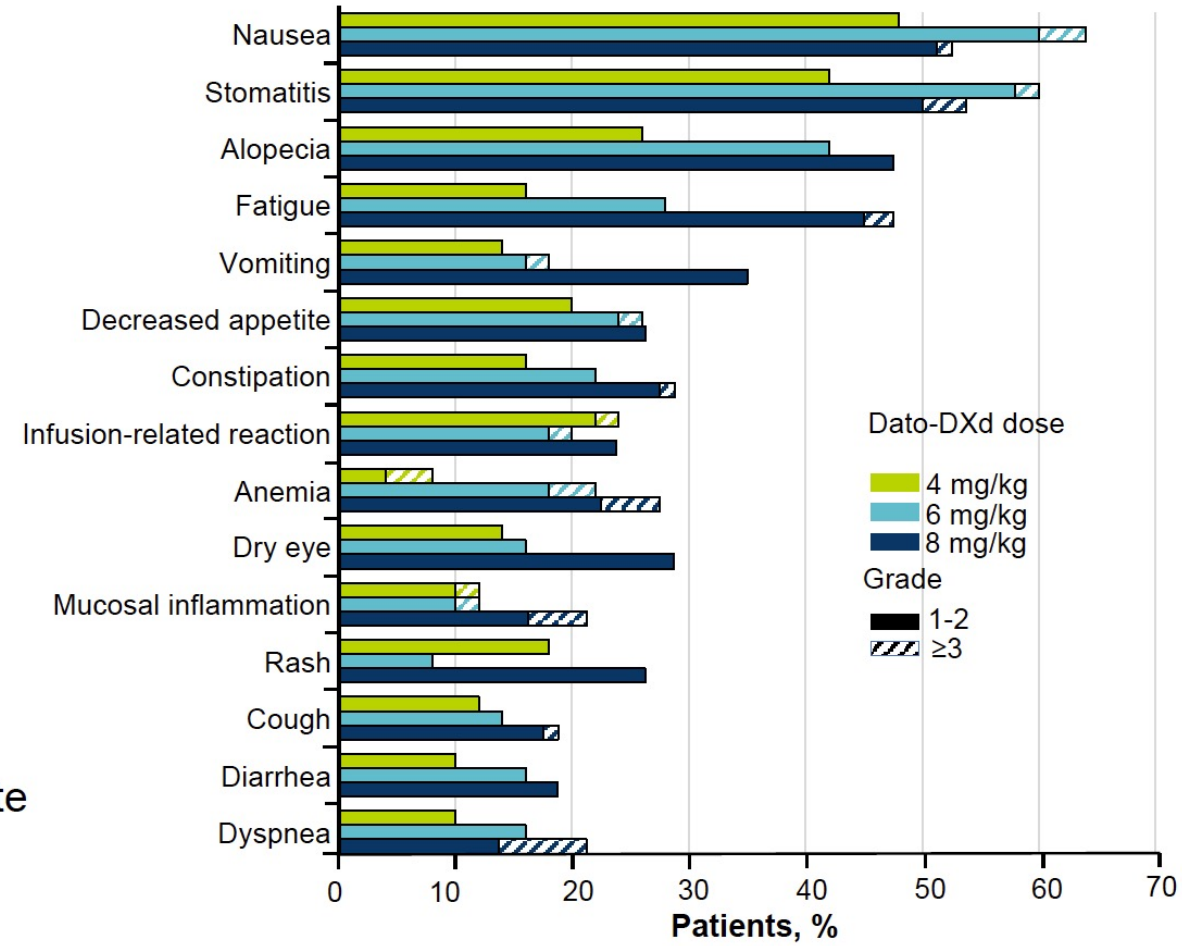
TROPION-PanTumor01: Safety Summary

Overall Safety Summary

Patients, n (%)	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
TEAE	49 (98)	49 (98)	80 (100)
Grade ≥3	15 (30)	27 (54)	46 (58)
Drug-related TEAE	47 (94)	41 (82)	78 (98)
Grade ≥3	7 (14)	13 (26)	28 (35)
Serious TEAE	10 (20)	24 (48)	40 (50)
Grade ≥3	10 (20)	18 (36)	37 (46)
Dose adjustments			
TEAEs associated with discontinuation	8 (16)	7 (14)	19 (24)
TEAEs associated with dose interruption	4 (8)	15 (30)	29 (36)
TEAEs associated with dose reduction	1 (2)	5 (10)	23 (29)
ILD adjudicated as drug related[a]	5 (10)	3 (6)	11 (14)
Grade ≤2	4 (8)	2 (4)	7 (9)
Grades 3-4	1 (2)	1 (2)	1 (1)
Grade 5	0	0	3 (4)

- The safety profile was manageable with mainly mild/moderate toxicity; TEAEs were primarily nonhematologic

TEAEs in ≥15% of Patients[b]



Data cutoff: April 6, 2021.
ILD, interstitial lung disease; TEAE, treatment-emergent adverse event.
[a] Cases of ILD adjudicated as drug related comprised 5 patients in the 4-mg/kg cohort (1 grade 1, 3 grade 2, 1 grade 3), 3 patients in the 6-mg/kg cohort (2 grade 2, 1 grade 4), and 11 patients in the 8-mg/kg cohort (2 grade 1, 5 grade 2, 1 grade 3, 3 grade 5). [b] Of 180 patients (4 mg/kg [n=50]; 6 mg/kg [n=50]; 8 mg/kg [n=80]).

Garon EB et al. World Conference on Lung Cancer 2021;Abstract MA03.02.

Questions — Kelly EH Goodwin, MSN, RN, ANP-BC

Patients with metastatic NSCLC and a HER2 mutation

- **What do you say to patients with metastatic NSCLC with HER2 mutation who are about to begin treatment with trastuzumab deruxtecan?**
- **How do you assess cardiopulmonary function in these patients, and what is your approach to monitoring during treatment?**
- **What are some of the psychosocial issues that arise in this situation?**

RTP
RESEARCH
TO PRACTICE

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

Patients with metastatic NSCLC and a HER2 mutation

- **Comprehensive chemotherapy teaching session to review schedule, logistics, treatment side effects, symptom management strategies and assessment of response**
  - **T-DXd side effects include fatigue, alopecia, nausea, vomiting, diarrhea, myelosuppression, elevated LFTs, as well as the rare but very serious side effects of decrement in EF and development of ILD.**
    - **Patients treated with 1+ prior lines of therapy may need upfront dose reduction, growth factor support, closer monitoring**
  - **Engage cardiologist or pulmonologist if patient already sees signs**
  - **Urge patients to call with respiratory changes, dizziness, fluid retention/weight gain**

RTP RESEARCH TO PRACTICE

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Baseline echocardiogram and q3 months while on active therapy**
- **Detailed history and physical prior to each dose**
  - **Optimize home supports and engage specialists for vitals/weight monitoring or if titrating diuretics or other chronic medications**
- **Reinforce need to call with new/worsening respiratory symptoms, fluid retention, dizziness**
  - **DDx include infection, pneumonitis, cardiac toxicity, disease progression**
  - **Urgent evaluation for new dyspnea, cough should include resting and exertional vitals, laboratory assessments (including pro-BNP), imaging**

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TO PRACTICE

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **73yo F, former smoker (15 pk yrs), PMH L breast CA s/p mastectomy and adjuvant chemotherapy 1993, AFib, anxiety and depression with incidentally found Stage 1A lung CA 6/2016, RLL wedge resection 6/2016, subsequently found to have FDG avid R hilar LN, biopsy proven N1 recurrence, underwent completion RLL lobectomy on 6/2017 and completed adjuvant chemotherapy (cis/pem x 3 and discontinued for intolerance).**
- **Metastatic recurrence in R lung, LNs, bones 7/2018, HER2 positive, treated with carbo/pem/pembro x 4 followed by maintenance pem/pembro then progression after 1 year.**

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Poziotinib clinical trial → discontinued for intolerance (fatigue, diarrhea, mucositis) → ADC to TROP2 Phase 1 clinical trial (DS-1062a) → progressed after 1 year → ineligible for trastuzumab deruxtecan clinical trial due to DS-1062a → Ado-trastuzumab emtansine (T-DM1) off-label → restaging scans with response but pneumonitis → responded to steroids, therapy discontinued → vinorelbine → oligoprogression with solitary liver lesion after ~8 months, treated with IR ablation and resumed vinorelbine → progression in Tspine after ~6 months, treated palliative RT and switched therapy to trastuzumab deruxtecan**
  - **Risk of recurrent, life-threatening pneumonitis reviewed; patient opted for close interval restaging s/p palliative RT and proceeded with T-DXd when scans showed further/considerable progression**
  - **Treatment complicated by fatigue, appetite changes, nausea/dry heaves, overall functional decline**

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Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

  - **Restaging scans with response but new RUL and LLL GGOs concerning for pneumonitis – treatment discontinued, patient trialed gemcitabine with poor tolerance and opted to enroll in hospice nearly 3 years after metastatic recurrence**

- **HER2 mutations more commonly associated with female, non-smokers, Asian descent**
  - **Families, work obligations for younger patients**
  - **Transportation, family supports, financial toxicity for older patients**
  - **Standard of care vs clinical trial participation – how to sequence therapy?**
  - **Anxiety associated with chronic illness – waiting for the other shoe to drop**
- **Managing expectations for patients with less common actionable mutations without first line or “miracle treatments” can be challenging**

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Agenda

Module 1 – Key Lung Cancer Diagnostic Tools

Module 2 – Targeted Therapy for Localized Disease

Module 3 – Targeted Treatment for Metastatic Disease

- EGFR activating mutations
- EGFR exon 20 insertion mutations
- ALK rearrangements
- RET fusions
- KRAS G12C mutations
- HER2 mutations
- Other targets in NSCLC (MET, ROS1, BRAF, NTRK, NRG1)

Module 4 – Immunotherapy for Localized Disease

Module 5 – Immunotherapy for Metastatic Disease

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Other Targetable Genomic Alterations in NSCLC

- **MET Exon 14 Skipping Mutations**
  - ***Capmatinib, tepotinib***
- **ROS1 Fusions**
  - ***Entrectinib, crizotinib, ceritinib***
- **BRAF Mutations**
  - ***Dabrafenib/trametinib, vemurafenib***
- **NTRK Fusions**
  - ***Entrectinib, larotrectinib, crizotinib***
- **NRG1 Fusions**
  - *Seribantumab (not FDA approved)*

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications
NCCN Guidelines Version 3.2022 Non-Small Cell Lung Cancer

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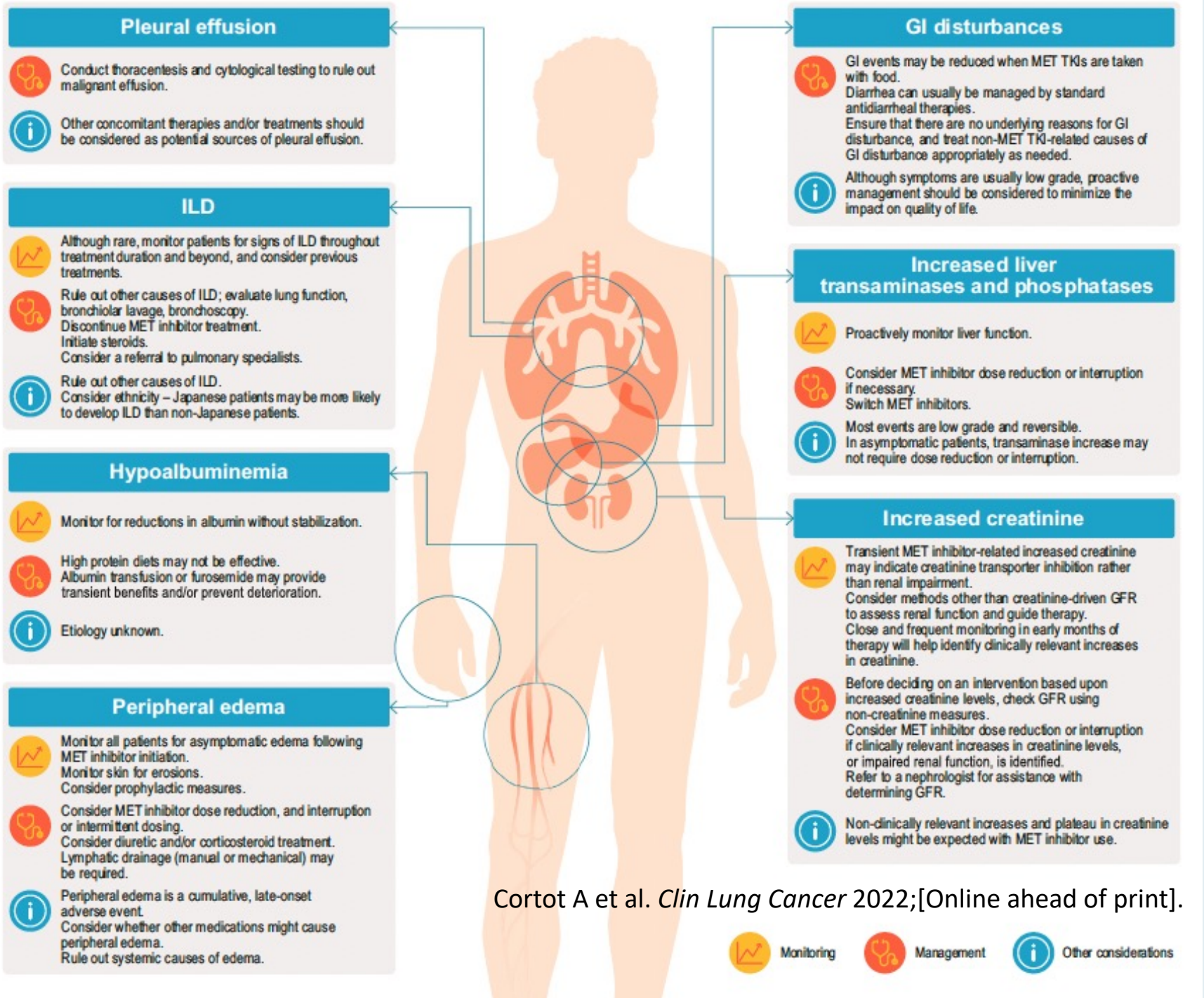

Cortot A et al. *Clin Lung Cancer* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Other Targetable Genomic Alterations in NSCLC

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NCCN Guidelines Version 3.2022 Non-Small Cell Lung Cancer

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Agenda

Module 1 – Key Lung Cancer Diagnostic Tools

Module 2 – Targeted Therapy for Localized Disease

Module 3 – Targeted Treatment for Metastatic Disease

Module 4 – Immunotherapy for Localized Disease

- Resectable localized NSCLC
- Locally advanced NSCLC

Module 5 – Immunotherapy for Metastatic Disease

RTP RESEARCH TO PRACTICE

SELF-ASSESSMENT QUIZ

Patients receiving anti-PD-1/PD-L1 antibodies may present with…

1. Hypothyroidism
2. Hyperthyroidism
3. Both
4. Neither
5. I don’t know

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SELF-ASSESSMENT QUIZ

Which of the following is a common issue with immune checkpoint inhibitors?

1. Thyroid dysfunction
2. Pituitary dysfunction
3. Nausea and vomiting
4. Hair loss
5. None of the above
6. I don’t know

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SELF-ASSESSMENT QUIZ

Which of the following is considered a contraindication to use of an immune checkpoint inhibitor?

1. Prior autoimmune disorder
2. Prior solid organ transplant
3. Both 1 and 2
4. Neither 1 nor 2
5. I don’t know

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.

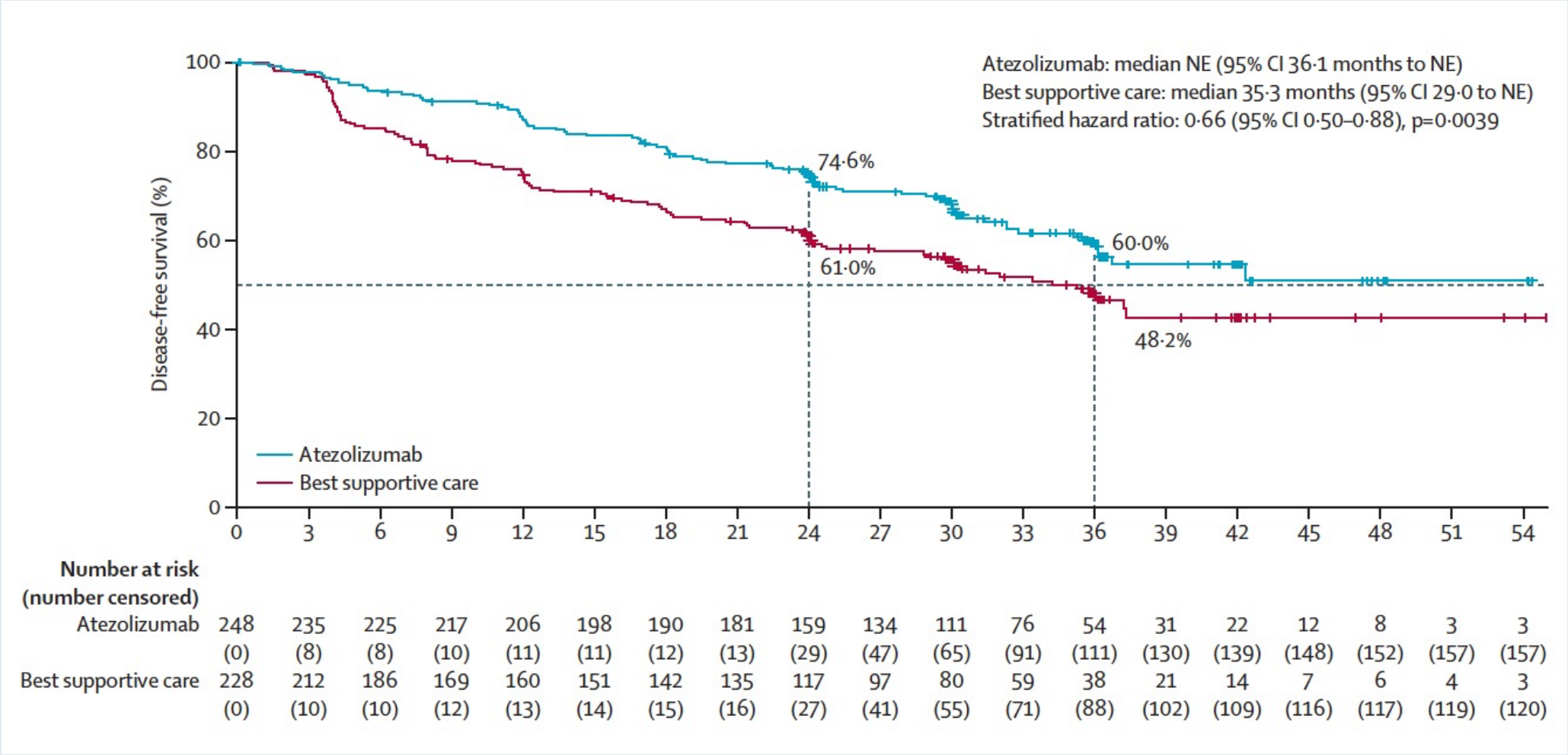
Today, the FDA also approved the VENTANA PD-L1 (SP263) Assay as a companion diagnostic device to select patients with NSCLC for adjuvant treatment with atezolizumab.

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 in patients on the atezolizumab arm compared with 35.3 months on the BSC arm (HR 0.66; p = 0.004). In a pre-specified secondary subgroup analysis of patients with PD-L1 TC ≥ 50% stage II-IIIA NSCLC, the DFS HR was 0.43. In an exploratory subgroup analysis of patients with PD-L1 TC 1-49% stage II-IIIA NSCLC, the DFS HR was 0.87.

The recommended atezolizumab dose for this indication is 840 mg every 2 weeks, 1,200 mg every 3 weeks, or 1,680 mg every 4 weeks for up to 1 year."

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

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



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

FDA Approves Neoadjuvant Nivolumab and Platinum-Doublet Chemotherapy for Localized NSCLC

Press Release – March 4, 2022

"The Food and Drug Administration approved nivolumab with platinum-doublet chemotherapy for adult patients with resectable non-small cell lung cancer (NSCLC) in the neoadjuvant setting. This represents the first FDA approval for neoadjuvant therapy for early-stage NSCLC.

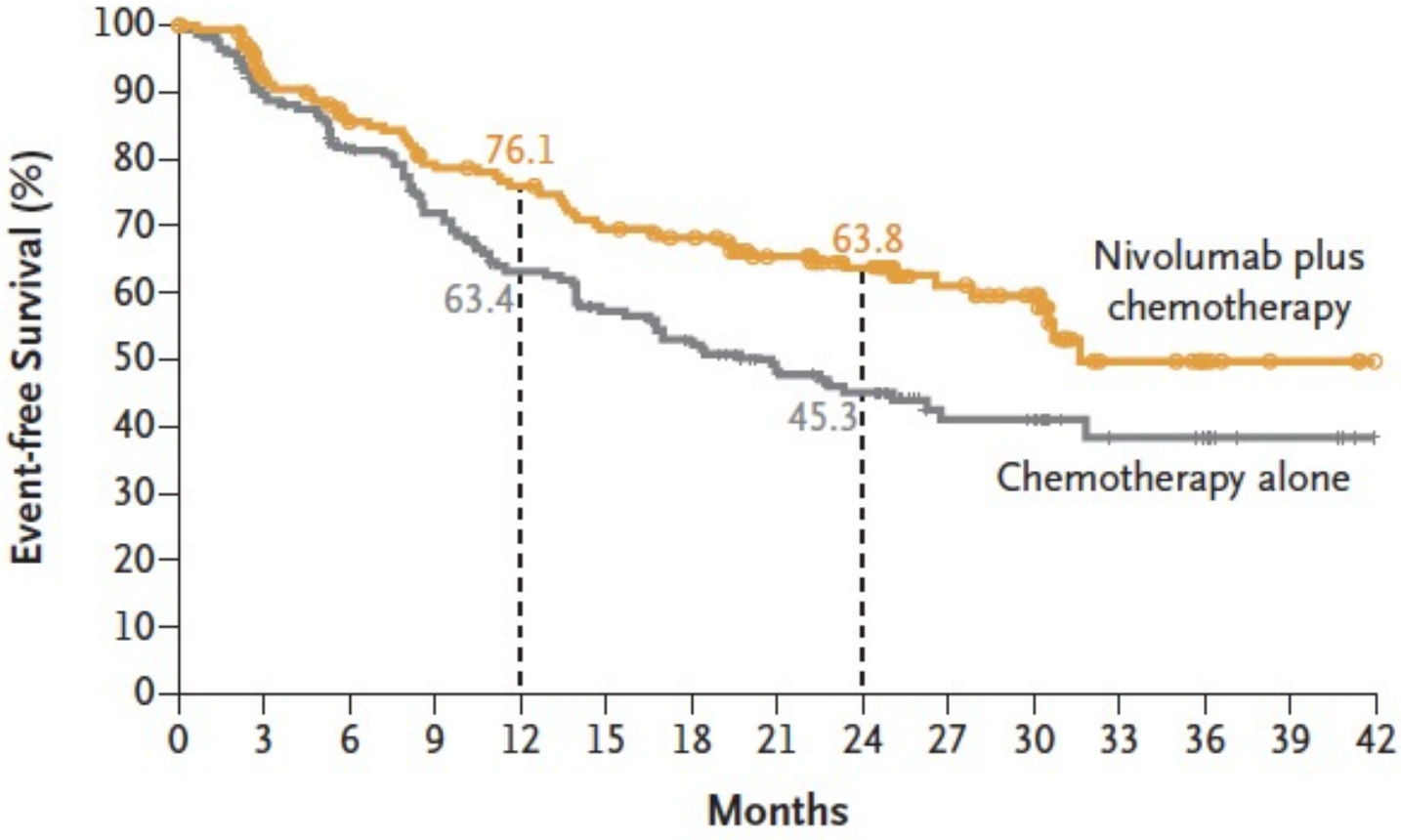
Efficacy was evaluated in CHECKMATE-816 (NCT02998528), a randomized, open label trial in patients with resectable, histologically confirmed Stage IB (≥4 cm), II, or IIIA NSCLC (AJCC/UICC staging criteria) and measurable disease (RECIST v1.1.). Patients were enrolled regardless of the tumor PD-L1 status. A total of 358 patients were randomized to receive either nivolumab plus platinum-doublet chemotherapy administered every 3 weeks for up to 3 cycles, or platinum-chemotherapy alone administered on the same schedule.

The main efficacy outcome measures were event-free survival (EFS) and pathologic complete response (pCR) by blinded independent central review. Median EFS was 31.6 months in the nivolumab plus chemotherapy arm and 20.8 months for those receiving chemotherapy alone. The hazard ratio was 0.63 (p = 0.0052). The pCR rate was 24% in the nivolumab plus chemotherapy arm and 2.2% in the chemotherapy alone arm."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-neoadjuvant-nivolumab-and-platinum-doublet-chemotherapy-early-stage-non-small-cell-lung

RTP RESEARCH TO PRACTICE

CheckMate 816 Coprimary Endpoint: Event-Free Survival with Neoadjuvant Nivolumab/Chemotherapy for Localized NSCLC

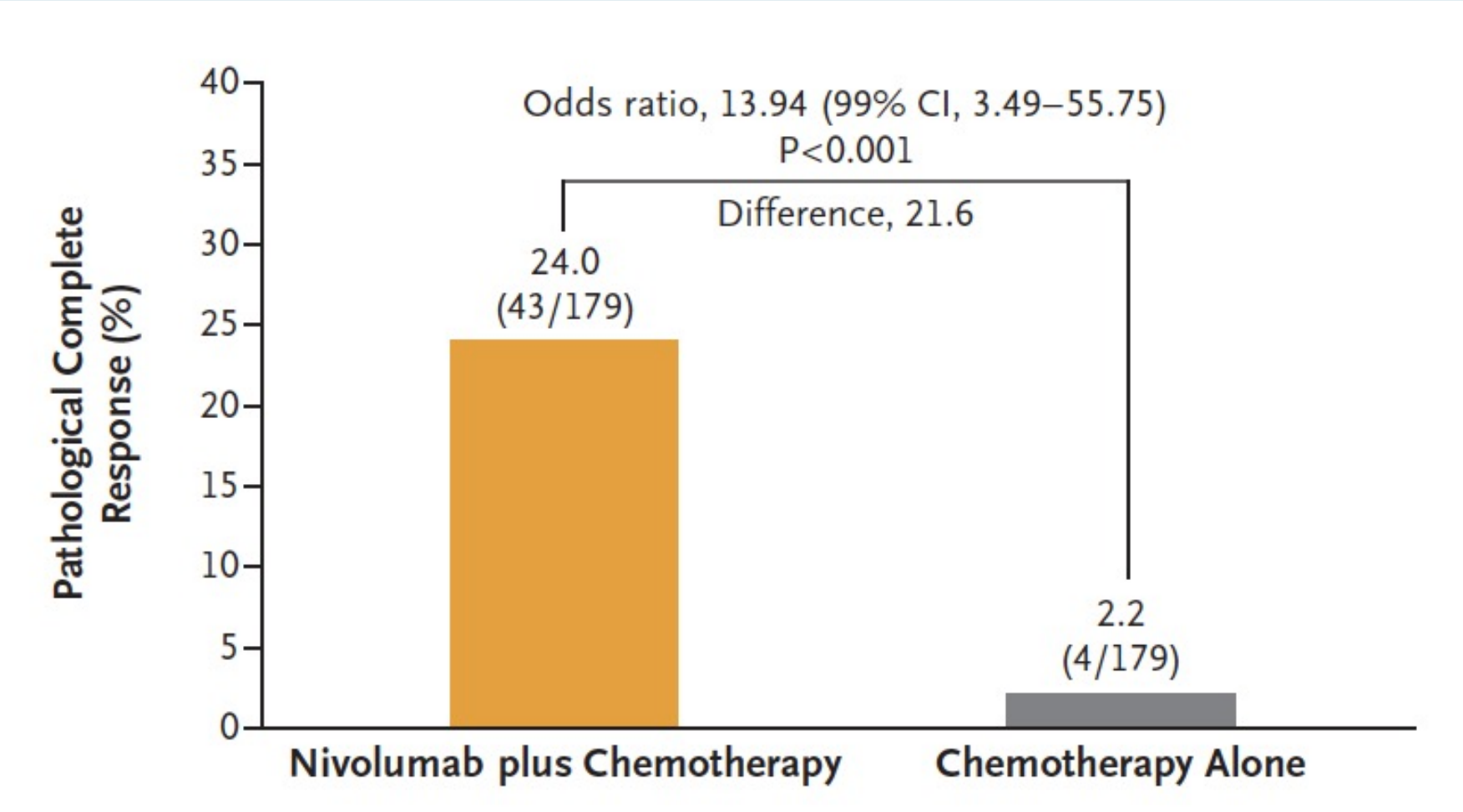


	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005

Forde PM et al. *N Engl J Med* 2022;[Online ahead of print].

CheckMate 816 Coprimary Endpoint: Pathologic Complete Response with Neoadjuvant Nivolumab/Chemotherapy for Localized NSCLC



Forde PM et al. *N Engl J Med* 2022;[Online ahead of print].

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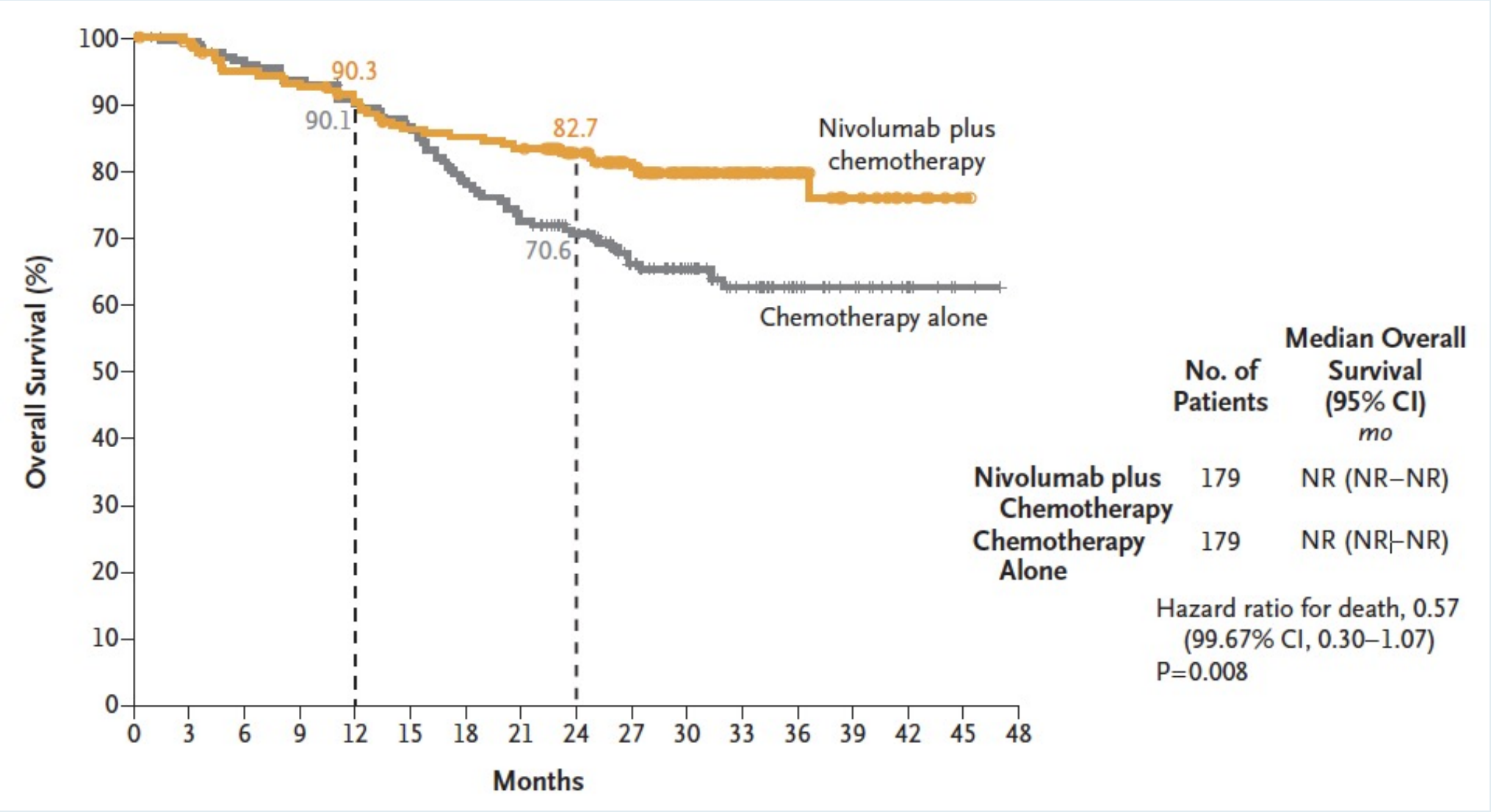
CheckMate 816: Overall Survival



	No. of Patients	Median Overall Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	NR (NR–NR)
Chemotherapy Alone	179	NR (NR–NR)

Hazard ratio for death, 0.57
(99.67% CI, 0.30–1.07)
P=0.008

Forde PM et al. *N Engl J Med* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Pembrolizumab Significantly Improves Disease-Free Survival versus Placebo as Adjuvant Therapy for Patients with Stage IB-IIIA NSCLC Regardless of PD-L1 Expression

Press Release – March 17, 2022

“Today [results were announced] from the pivotal Phase 3 KEYNOTE-091 trial, also known as EORTC-1416-LCG/ETOP-8-15 – PEARLS. The study found that adjuvant treatment with pembrolizumab significantly improved disease-free survival (DFS), one of the dual primary endpoints, reducing the risk of disease recurrence or death by 24% compared to placebo (hazard ratio [HR] = 0.76; p = 0.0014) in patients with stage IB (≥4 centimeters) to IIIA non-small cell lung cancer (NSCLC) following surgical resection regardless of PD-L1 expression. Median DFS was 53.6 months for pembrolizumab versus 42.0 months for placebo, an improvement of nearly one year. These data are being presented today during a European Society for Medical Oncology (ESMO) Virtual Plenary and will be shared with regulatory authorities worldwide.

'These are the first positive results for pembrolizumab in the adjuvant setting for non-small cell lung cancer, and represent the sixth positive pivotal study evaluating a pembrolizumab regimen in earlier stages of cancer,' said Dr Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories.

'Pembrolizumab has become foundational in the treatment of metastatic non-small cell lung cancer, and we are pleased to present these data showing the potential of pembrolizumab to help more patients with lung cancer in earlier stages of disease. We thank the patients, their caregivers and investigators for participating in this study.'”

https://finance.yahoo.com/news/merck-keytruda-pembrolizumab-significantly-improved-181500060.html

Symptoms of Immunotherapy Toxicity

Hypophysitis
(fatigue)

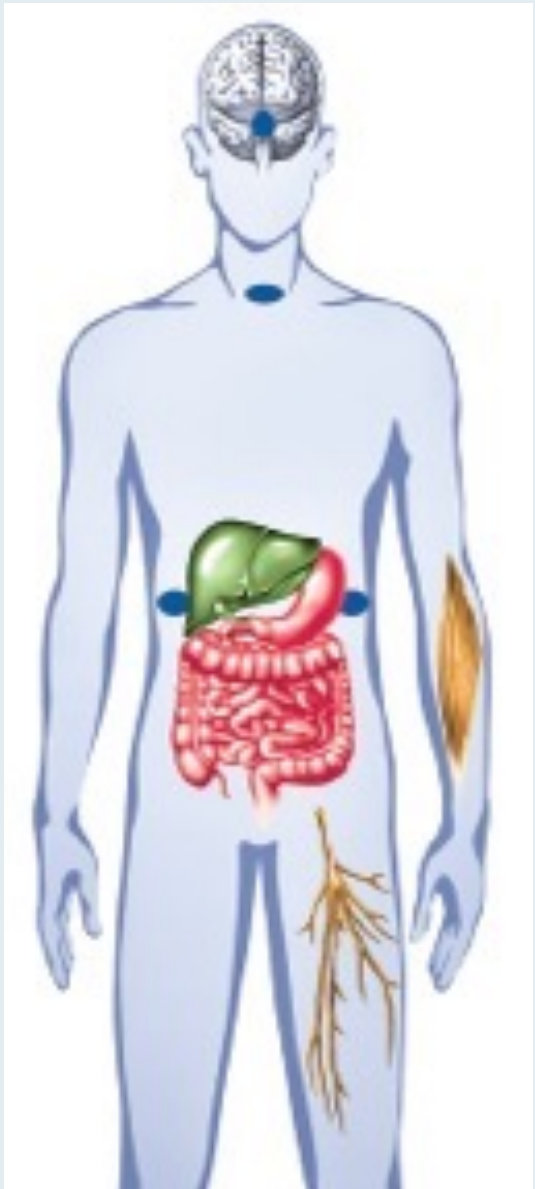
Thyroiditis
(over/underactive thyroid)

Adrenal Insufficiency
(fatigue)

Diabetes Mellitus
(Type I, II, fatigue, DKA)

Colitis
(diarrhea, abdominal pain)

Dermatitis
(rash, itch, blistering)



Pneumonitis
(dyspnea, cough)

Myocarditis
(chest pain, dyspnea)

Hepatitis
(abnornal LFTs, jaundice)

Pancreatitis
(abdominal pain)

Neurotoxicities
(MG, encephalitis)

Arthritis
(joint pain)

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Questions — Kelly EH Goodwin, MSN, RN, ANP-BC

Patients with localized NSCLC and no targetable mutations

- **What do you say to patients with NSCLC who are about to receive immunotherapy in terms of side effects and toxicities?**

- **What are some of the psychosocial issues that arise in this situation?**

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

Patients with localized NSCLC and no targetable mutations

- **CheckMate 816 (neoadjuvant platinum-based chemotherapy + nivolumab) and IMpower 010 (surgery upfront then adjuvant platinum-based chemo then adjuvant atezo)**
- **After recovery from side effects and restaging scans confirm no progression of disease, embark on 1 year of adjuvant immunotherapy**
  - **Decrease chance of recurrence and increase potential for cure – “insurance policy”**
  - **Treatment administered q2 or q4 weeks with surveillance scans q3 months or as clinically indicated**
  - **Unlike chemotherapy which kills indiscriminately, immunotherapy works by revving up the immune system and “uncloaking” cancer cells**
  - **Chemotherapy side effects more predictable in timeline and severity than IO toxicity**

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Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Immunotherapy toxicity can occur after a single dose, after many months/years or several months after therapy completed**
  - **Can be mild or life threatening**
    - **Can be temporary or permanent**
      - **Treated with steroids or other immune modulating drugs**
      - **Low threshold to call with any new symptoms**
- **"-itis" – side effects include fatigue, infusion reactions, neurological complaints, endocrinopathies, thyroid dysfunction, pneumonitis, myocarditis, gastritis, hepatitis, nephritis, colitis, arthralgias, myositis, itching/rash**
  - **Referral to SIC (Severe Immunotherapy Complications) service or other specialists**

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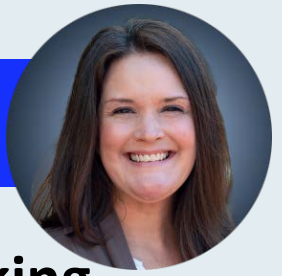
Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC



- **Logistics/care coordination with concurrent chemoRT – transportation/parking, home supports, balance recovery from chemoRT toxicity and initiation of IO**
- **Change in routine can be distressing – frequent/daily visits and predictable schedule/toxicities to monthly visits and less predictable side effects**
  - **Treatment toxicities can persist well beyond treatment completion – can be nuisance or life-altering/life-threatening**
- **Anxiety of surveillance scans and risk of local or metastatic recurrence**
  - **Lifestyle modification**

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Agenda

Module 1 – Key Lung Cancer Diagnostic Tools

Module 2 – Targeted Therapy for Localized Disease

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- Resectable localized NSCLC
- Locally advanced NSCLC

Module 5 – Immunotherapy for Metastatic Disease

SELF-ASSESSMENT QUIZ

The survival benefit of durvalumab consolidation after chemoradiation therapy for patients with locally advanced NSCLC…

1. Continues for at least 5 years
2. Drops off with time
3. Continues for about 2 years and then drops off
4. I don’t know

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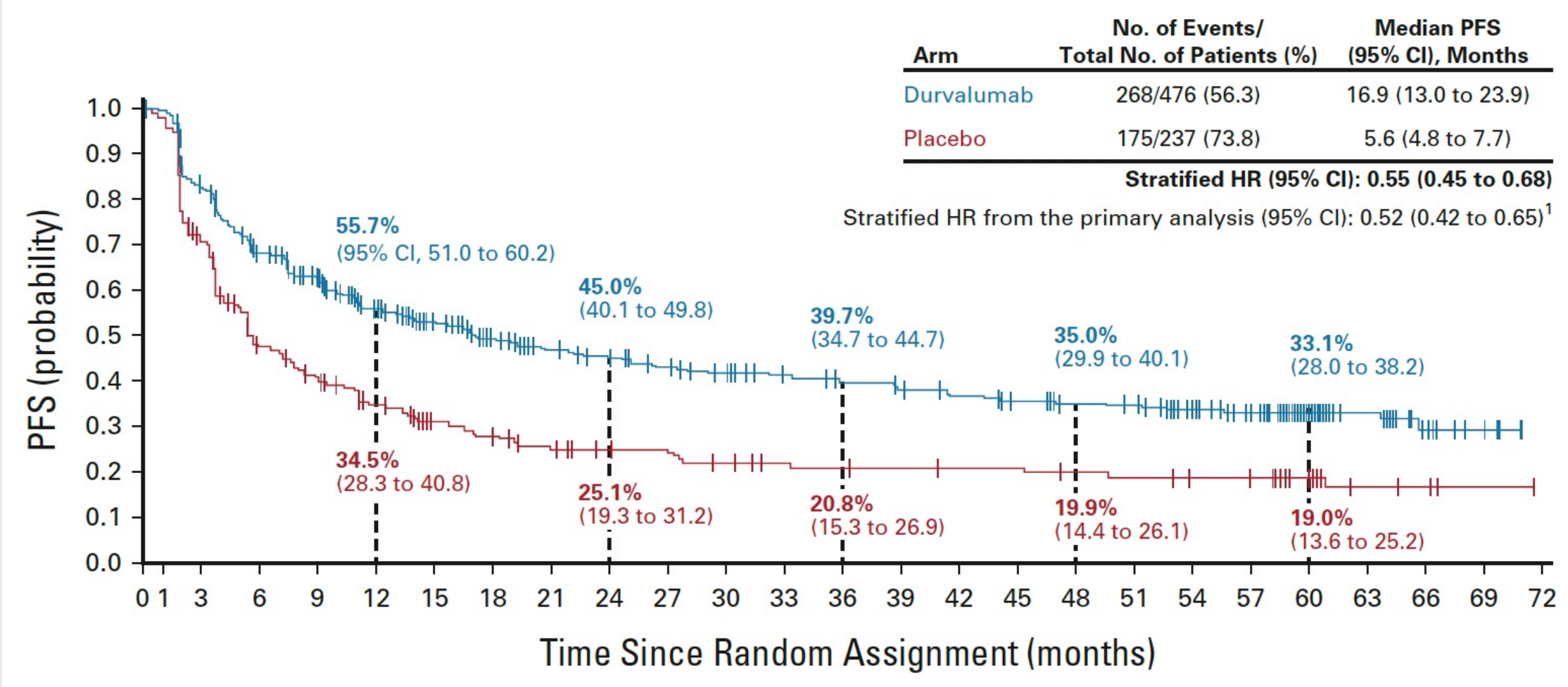
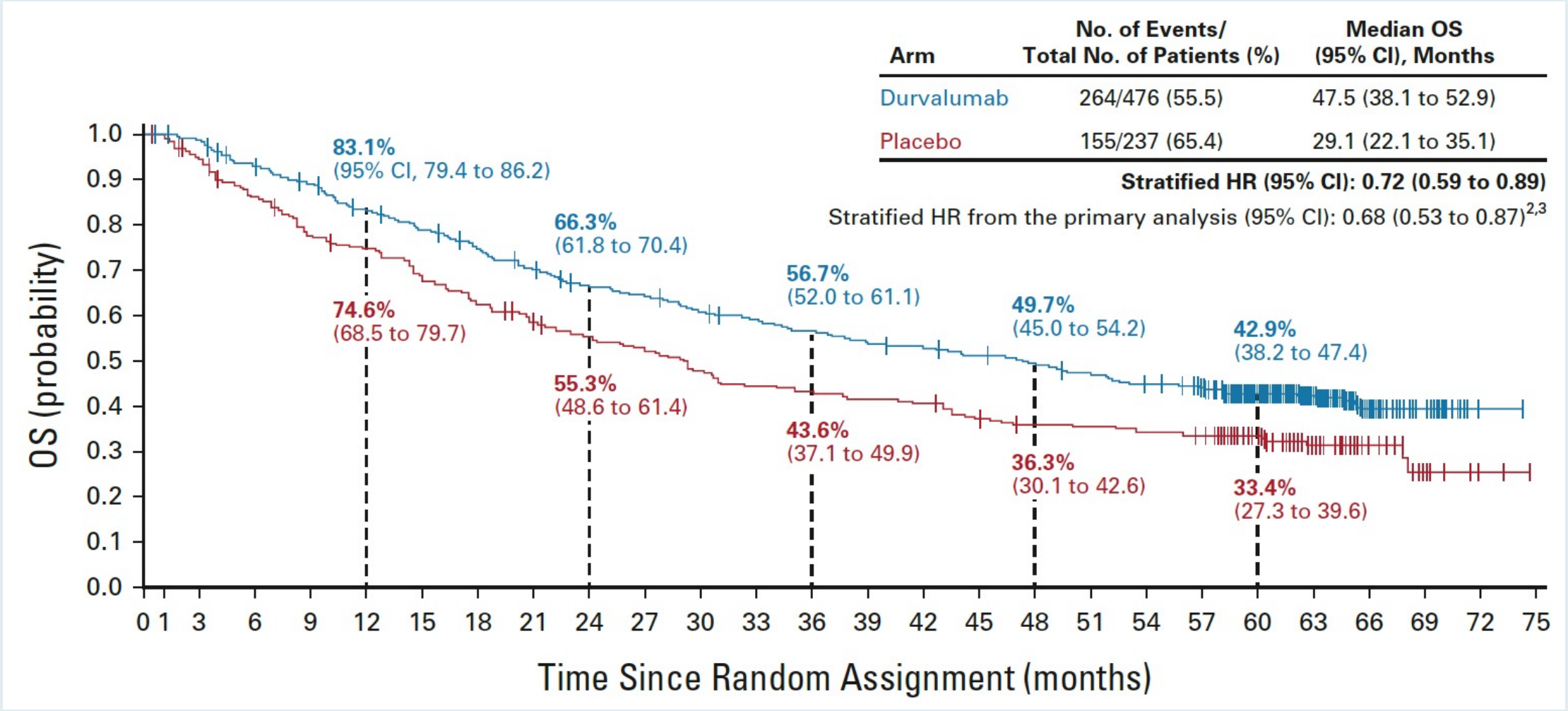
PACIFIC: Five-Year Progression-Free Survival (PFS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



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].

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Questions — Anne S Tsao, MD, MBA

Patients with localized nonsquamous NSCLC, PD-L1 TPS 90% and no targetable mutations

- **What therapies are used in this setting, and how is treatment selected?**
- **Please cite brief instructive examples of actual clinical experiences with patients in your practice.**

Unresectable Local-Regionally Advanced NSCLC (LA-NSCLC) Guidelines

- **LA-NSCLC can be cured with multimodality therapy.**
- **Stage III NSCLC is heterogeneous, and individualized therapy is necessary to optimize cure.**
- **Unresectable disease: Standard dose fractionation of XRT is 60 Gy given in 2-Gy once-daily fractions over 6 weeks concurrent with chemotherapy.**
- **PACIFIC trial established that 1 year of durvalumab after definitive concurrent chemoradiation (+/- neoadjuvant therapy) improved survival and is the standard.**

Bezjak et al. JCO 33 (18):2100-2105, 2015; Antonia S, et al. NEJM 377 (20): 1919-1929, Nov 2017; Antonia S et al. NEJM 379 (24): 2342-2350, Dec 2018

Stage III NSCLC Is Heterogeneous
FUTURE: Personalized Therapy Is Essential

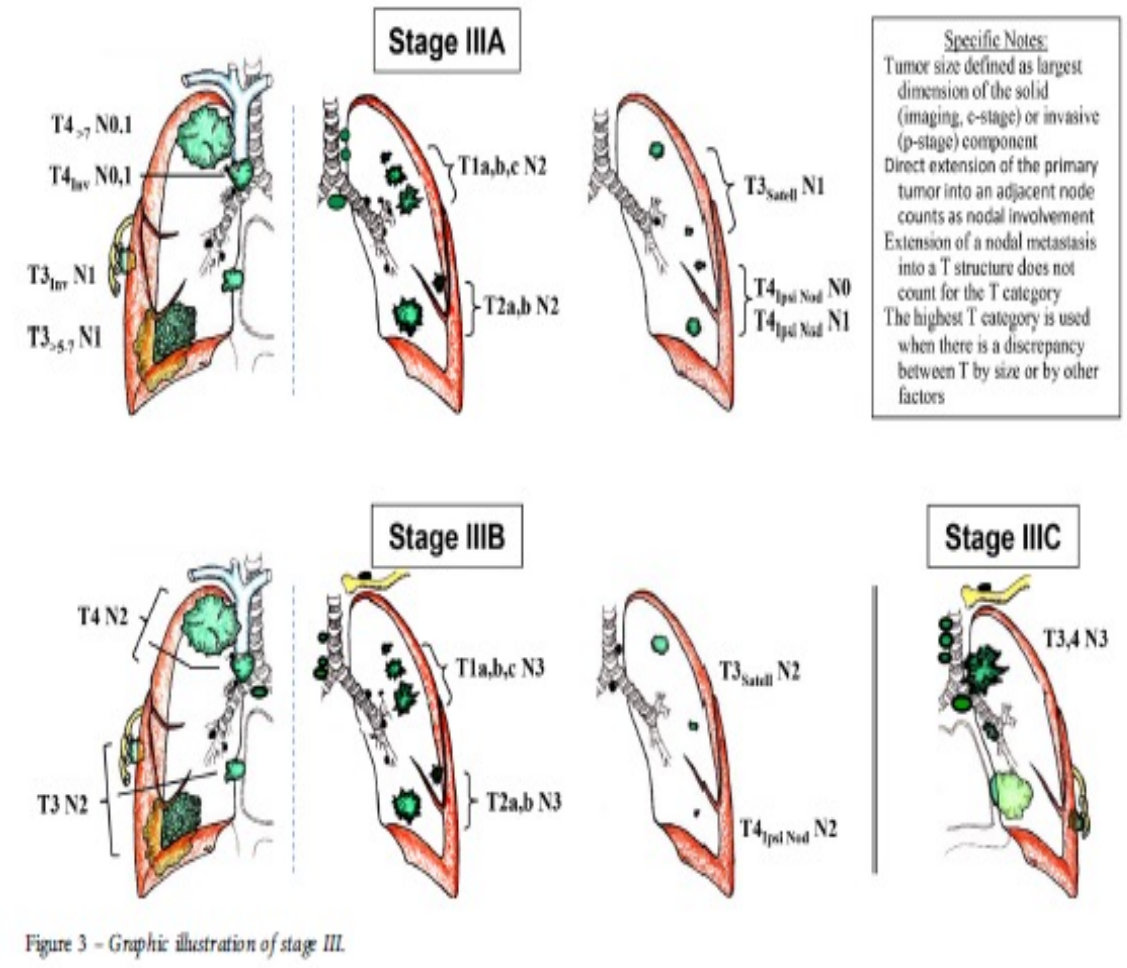

Figure 3 – Graphic illustration of stage III.

Hypothetical Future Strategies

Unresectable Large T or N3 or Bulky or multi-station N2 LN	Neoadjuvant chemo-immunotherapy Concurrent immuno-radiation then 1 year immunotherapy
Small T, **PD-L1 IHC high,** small multi-station N2 LN	Concurrent immuno-radiation then 1 year immunotherapy
Small T, PD-L1 IHC low, small multi-station N2 LN	Concurrent chemo-radiation then 1 year immunotherapy
Large T Single-station N2 LN	Neoadjuvant chemo-immunotherapy, Surgery +/- XRT, then 1 year immunotherapy
Small T Single-station N2 LN	Neoadjuvant immunotherapy, Surgery +/- XRT, then 1 year immunotherapy

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Detterbeck et al. 8th Edition Lung Cancer Stage Classification, Chest 151 (1): 193-203, 2017

Questions — Tara Plues, APRN, MSN

Patients with locally advanced NSCLC

- **What do you say to patients who are about to initiate treatment with durvalumab consolidation in terms of what they should expect?**
- **What are some of the psychosocial issues that arise in this situation?**

Commentary — Tara Plues, APRN, MSN

Patients with locally advanced NSCLC

- **What do you say to patients who are about to initiate treatment with durvalumab consolidation in terms of what they should expect with this treatment?**
- **Single agent immunotherapy, and specifically durvalumab, is generally well tolerated. The most common side effects are mild in nature and include fatigue, itching, rashes and muscle/joint aches. The more significant side effects are rare, but are still possible and we will monitor closely for those. I don't like to give a long list of those things because it can be overwhelming, but if you develop any new symptoms I would like for you to call me and let me know so I can assess them.**

RTP RESEARCH TO PRACTICE

Commentary — Tara Plues, APRN, MSN

- **One example is a 60 year old female diagnosed with stage IB NSCLC with a local left hilar recurrence 18 months after right upper lobectomy. She received concurrent chemoXRT with weekly paclitaxel/carboplatin followed by adjuvant durvalumab.**
- **Phmx includes DM, obesity, mitral valve disorder, TIA, migraines, osteoarthritis, COPD**
- **Early on in durvalumab treatments she developed slowly worsening dyspnea on exertion.**
  - **XRT pneumonitis?**
  - **COPD?**
  - **irAE?**

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Commentary — Tara Plues, APRN, MSN

- **Tried ipratropium bromide/albuterol. No significant relief. Chest CT performed, revealed focal ground glass opacities in the XRT field. We felt that the symptoms were likely XRT pneumonitis with possibly some COPD exacerbation component as well. Decision was made to start prednisone at 40 mg daily and hold treatment for 1 cycle. We weaned down to 10 mg over a few weeks and restarted the durvalumab. Stayed on 10 mg prednisone daily for 4 months then stopped.**
- **The patient was very receptive to help. Worked very hard with exercise, pulmonary medicine visits, pulmonary rehab, weight loss. She made huge improvements in her quality of life.**

Commentary — Tara Plues, APRN, MSN

What are some of the psychosocial issues that arise in these situations?

- **Dealing with other diagnoses/comorbidities. In this situation, this patient was working hard at managing her diabetes and her weight in an effort to improve her breathing and overall state of health.**
- **Sometimes having cancer or being on treatment can be a self-fulfilling prophecy. People expect that they are not going to feel well before it starts. I was really proud of this patient and how hard she tried, she really pushed herself outside her comfort zone to make improvements. This was during an already challenging time in her life and she overcame several obstacles.**

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Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **76yo M, former smoker (80 pk yrs), PMH of melanoma, GERD, HTN, hyperlipidemia, COPD, alcohol dependence, hearing loss, memory issues, chronic fatigue, tinnitus, neuropathy and multiple lung CAs since 2005 (s/p resection, SBRT, cryoablation) with increasing L aortopulmonic LN 5/2021. No distant disease on PET. Stage III involvement, presumably from previously treated LLL cancer**
  - **Plan for definitive treatment with concurrent chemoRT with weekly carbo/paclitaxel followed by durvalumab as per PACIFIC.**
  - **Tolerated therapy well with minimal worsening of chronic fatigue and mild esophagitis; initiated durvalumab 3 weeks after completion of chemoRT**
  - **Currently 8 months into durvalumab and tolerating well with some anticipated dry skin and itching**
    - **Thick emollients, limiting sun exposure; rare antihistamines or hydroxyzine for itching; follows up with dermatologist**

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **57yo F, current smoker (0.25ppd) PMH obesity, GERD, multiple psychiatric disorders (major depressive disorder, anxiety, OCD, ADHD), CVA (1999), anti-phospholipid antibody syndrome, avascular necrosis R hip, chronic pain syndrome, presents to ED with severe LUE pain late summer 2021 and found to have large LUL mass and mediastinal adenopathy. Also with new LUE DVT despite therapeutic warfarin. Workup reveals locally advanced disease, pathology most consistent with large cell neuroendocrine.**
  - **Treated concurrent chemoRT with cis/etop x 4 cycles (maximize chemotherapy to cover possible component of SCLC)**
  - **Durvalumab per PACIFIC**
    - **APLS not a clear contraindication for IO per hematologist; discussion of benefits/risks with patient and companion**
      - **Case reports IO causing APLS; mixed data of increased thromboembolic events on IO in setting of APLS**

RTP RESEARCH TO PRACTICE

Commentary — Kelly EH Goodwin, MSN, RN, ANP-BC

- **Initiated IO 12/2021, tolerated well, plan for q2 weeks through first surveillance scan then transition to q4 week administration**
  - **Surveillance scans late 2/2022 without recurrence but reported mild nausea x 1 week, decision to continue q2 week treatment to monitor closely. No-showed to next visit and rescheduled visit, ultimately presented to clinic with c/o worsening nausea, dizziness, confusion and found to have multiple new large brain mets (5 lesions 1.2cm-2.6cm with associated edema). Underwent surgical resection of largest cerebellar met 4/13/22 and planning WBRT then systemic therapy.**

Agenda

Module 1 – Key Lung Cancer Diagnostic Tools

Module 2 – Targeted Therapy for Localized Disease

Module 3 – Targeted Treatment for Metastatic Disease

Module 4 – Immunotherapy for Localized Disease

Module 5 – Immunotherapy for Metastatic Disease

RTP RESEARCH TO PRACTICE

SELF-ASSESSMENT QUIZ

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

1. Agree
2. Disagree
3. I don’t know

Key Considerations

- Squamous versus nonsquamous histology
- PD-L1 levels; tumor mutation burden
- Chemotherapy versus chemoimmunotherapy as up-front treatment
- Chemotherapy with or without chemoimmunotherapy with or without bevacizumab
- Chemotherapy versus anti-PD-1/anti-CTLA-4 antibody

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 SK et al. *Lancet* 2019;393(10183):1829-30. [2] Reck M et al. *J Clin Oncol* 2019;37(7):537-46.
[3] Herbst RS et al. *N Engl J Med* 2020;383(14):1328-39. [4] Sezer A et al. *Lancet* 2021;397(10274):592-604.

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 D et al. *Ann Oncol* 2021;32(7):881-95. [2] Paz-Ares L et al. *J Thorac Oncol* 2020;15(10):1657-69.
[3] Socinski MA et al. *J Thorac Oncol* 2021;16(11):1909-24. [4] West H et al. *Lancet Oncol* 2019;20(7):924-37.
[5] Paz-Ares LG et al. ASCO 2021;Abstract 9016. [6] Reck M et al. ASCO 2021;Abstract 9000.

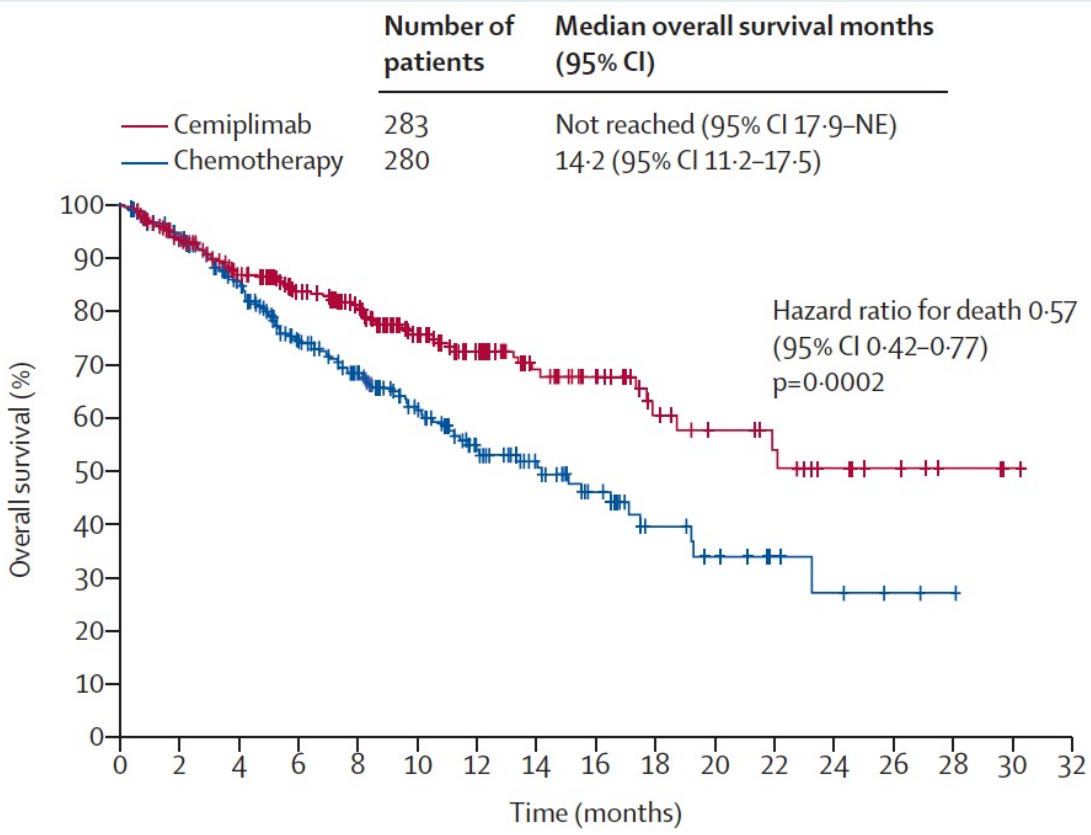
Lancet 2021;397:592-604.

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

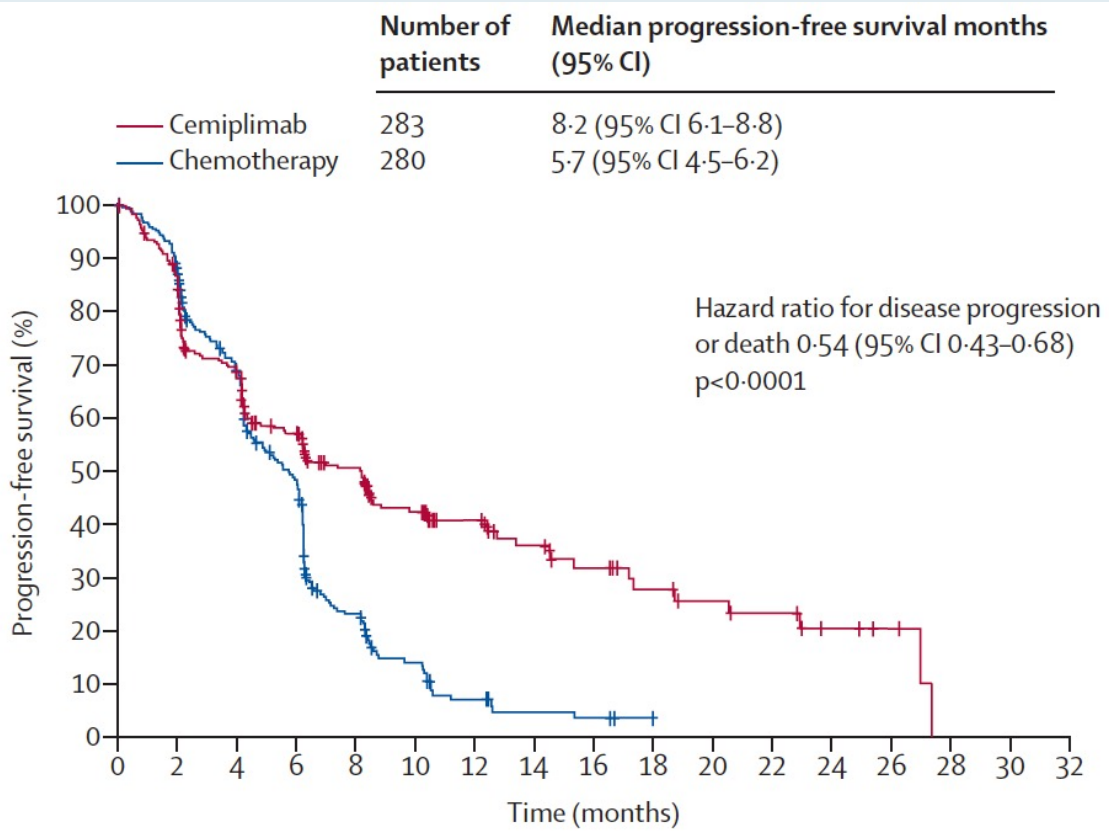
Ahmet Sezer, Saadettin Kilickap, Mahmut Gümüş, Igor Bondarenko, Mustafa Özgüroğlu, Miranda Gogishvili, Haci M Turk, Irfan Cicin, Dmitry Bentsion, Oleg Gladkov, Philip Clingan, Virote Sriuranpong, Naiyer Rizvi, Bo Gao, Siyu Li, Sue Lee, Kristina McGuire, Chieh-I Chen, Tamta Makharadze, Semra Paydas, Marina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

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

Overall Survival



Progression-Free Survival



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

2021 ESMO congress **Abstract LBA51**

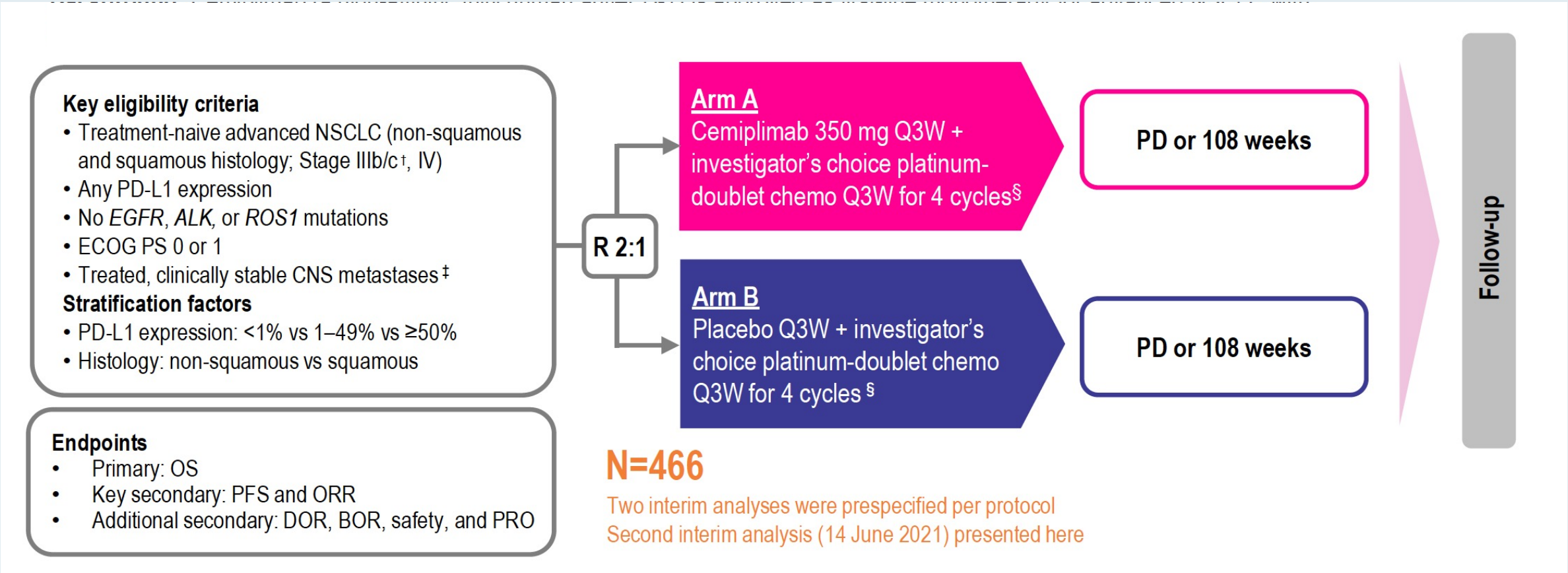
EMPOWER

EMPOWER-Lung 3: Cemiplimab in Combination With Platinum-Doublet Chemotherapy (Chemo) for First-Line (1L) Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC)

Miranda Gogishvili,[1] Tamar Melkadze,[2] Tamta Makharadze,[3] David Giorgadze,[4] Mikhail Dvorkin,[5] Konstantin Penkov,[6] Konstantin Laktionov,[7] Gia Nemsadze,[8] Marina Nechaeva,[9] Irina Rozhkova,[10] Ewa Kalinka,[11] Christian Gessner,[12] Brizio Moreno-Jaime,[13] Rodolfo Passalacqua,[14] Siyu Li,[15] Kristina McGuire,[15] Ruben G. W. Quek,[15] Bo Gao,[15] Frank Seebach,[15] David M. Weinreich,[15] George D. Yancopoulos,[15] Israel Lowy,[15] Giuseppe Gullo,[15] Petra Rietschel[15]

[1]High Technology Medical Centre, University Clinic Ltd, Tbilisi, Georgia; [2]Georgia Medical Institute, Jonesboro, Georgia, USA; [3]LTD High Technology Hospital Med Center, Batumi, Georgia; [4]David Tvildiani Medical University, Tbilisi, Georgia; [5]State Budgetary Healthcare Institution of Omsk Region, Omsk, Russia; [6]Private Medical Institution Euromedservice, St Petersburg, Russia; [7]Federal State Budgetary Institution "N.N. Blokhin National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia; [8]The Institute of Clinical Oncology, Tbilisi, Georgia; [9]Chelyabinsk Regional Clinical Oncology Center, Chelyabinsk, Chelyabinsk Oblast, Russia; [10]State Budgetary Healthcare Institution of Kaluga Region, Kaluga, Russia; [11]Polish Mother's Memorial Hospital Research Institute, Łódź, Poland; [12]POIS Leipzig GbR Steffi Geßner, Leipzig, Germany; [13] Hospital Regional ISSSTE, León, Mexico; [14]Istituti Ospitalieri Di Cremona, Cremona, Italy; [15]Regeneron Pharmaceuticals, Inc, Tarrytown, New York

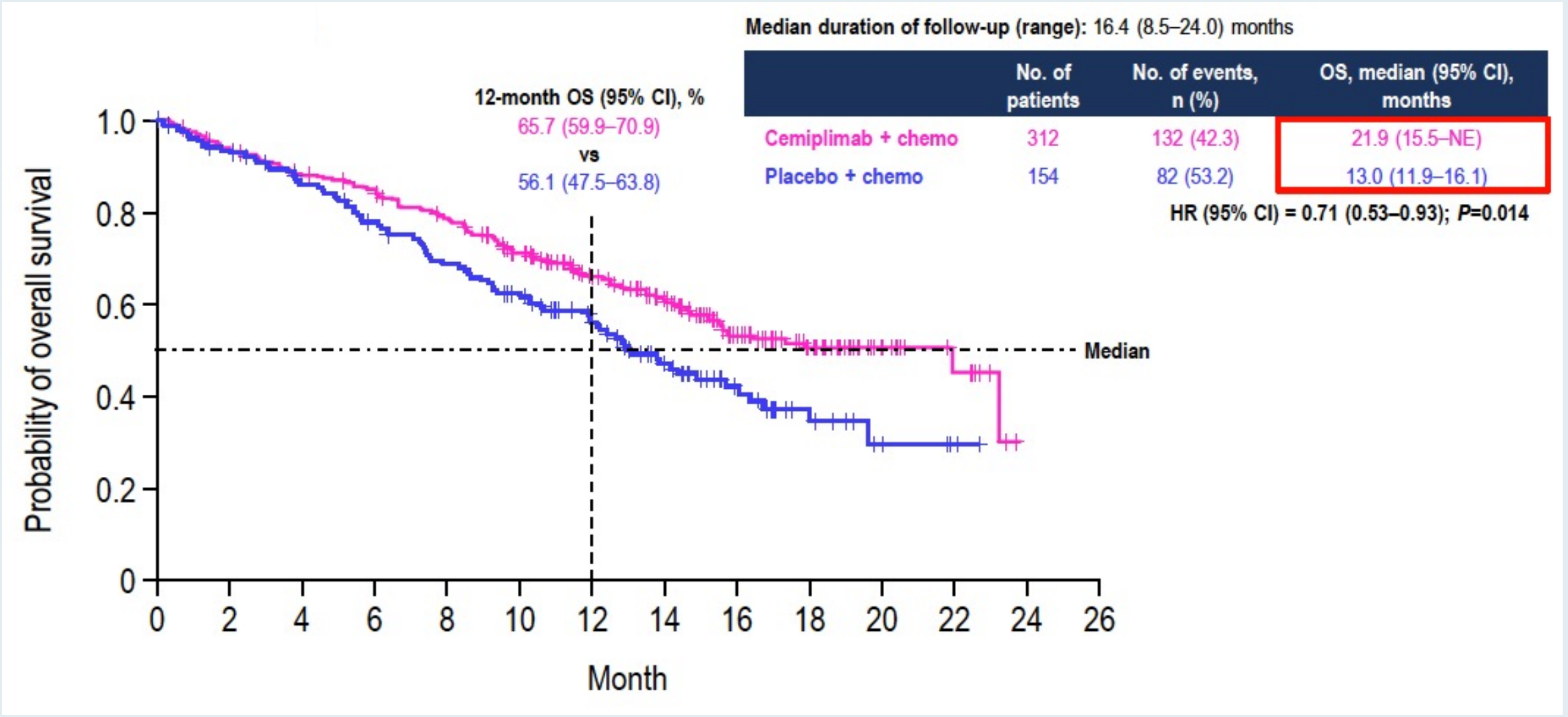
EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC



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



	No. of patients	No. of events, n (%)	OS, median (95% CI), months
Cemiplimab + chemo	312	132 (42.3)	21.9 (15.5–NE)
Placebo + chemo	154	82 (53.2)	13.0 (11.9–16.1)

HR (95% CI) = 0.71 (0.53–0.93); *P*=0.014

Gogishvili M et al. ESMO 2021;Abstract LBA51.

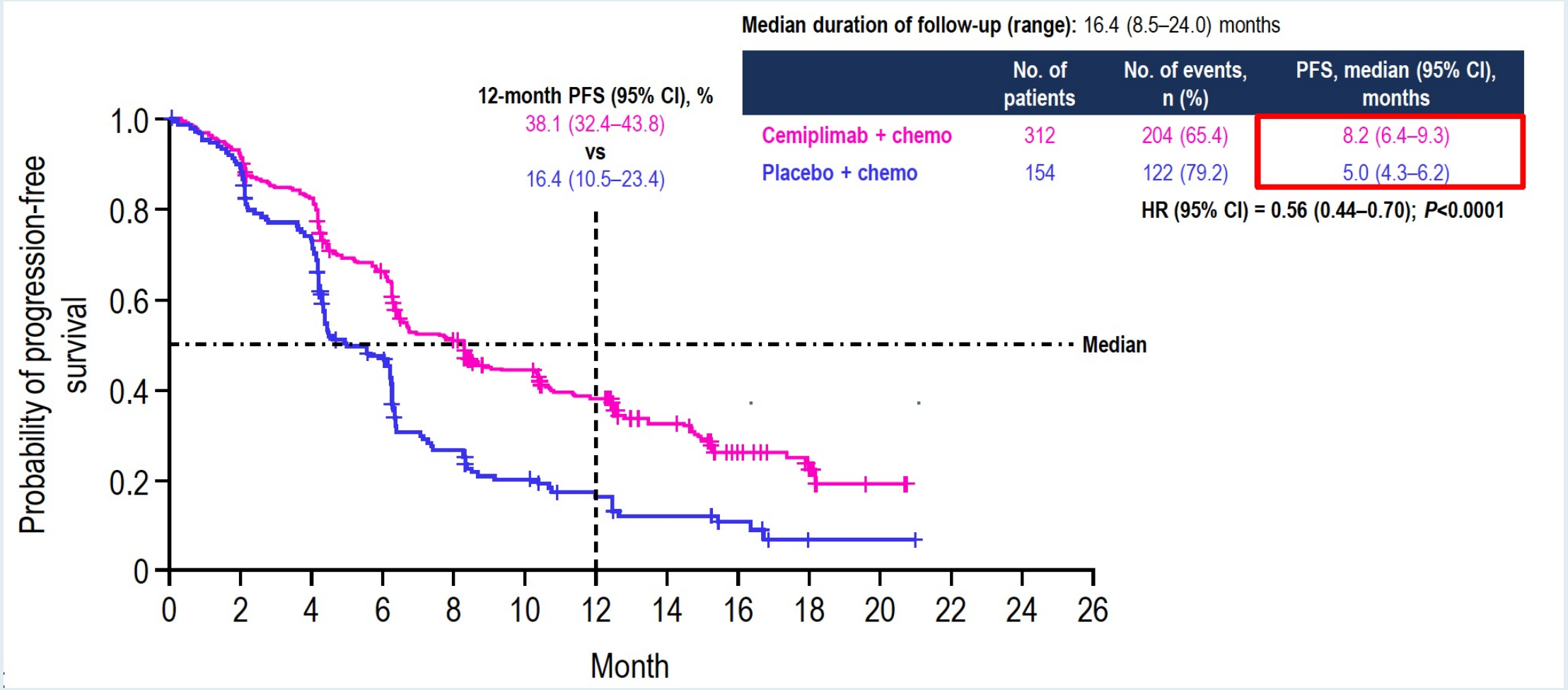
RTP RESEARCH TO PRACTICE

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.

Questions — Edward B Garon, MD, MS

Patients with metastatic nonsquamous NSCLC, PD-L1 TPS 90% and no targetable mutations

- **What therapies are used to treat NSCLC in this setting, and how is treatment selected?**

Commentary – Edward B Garon, MD, MS

Patients with metastatic nonsquamous NSCLC, PD-L1 TPS 90% and no targetable mutations

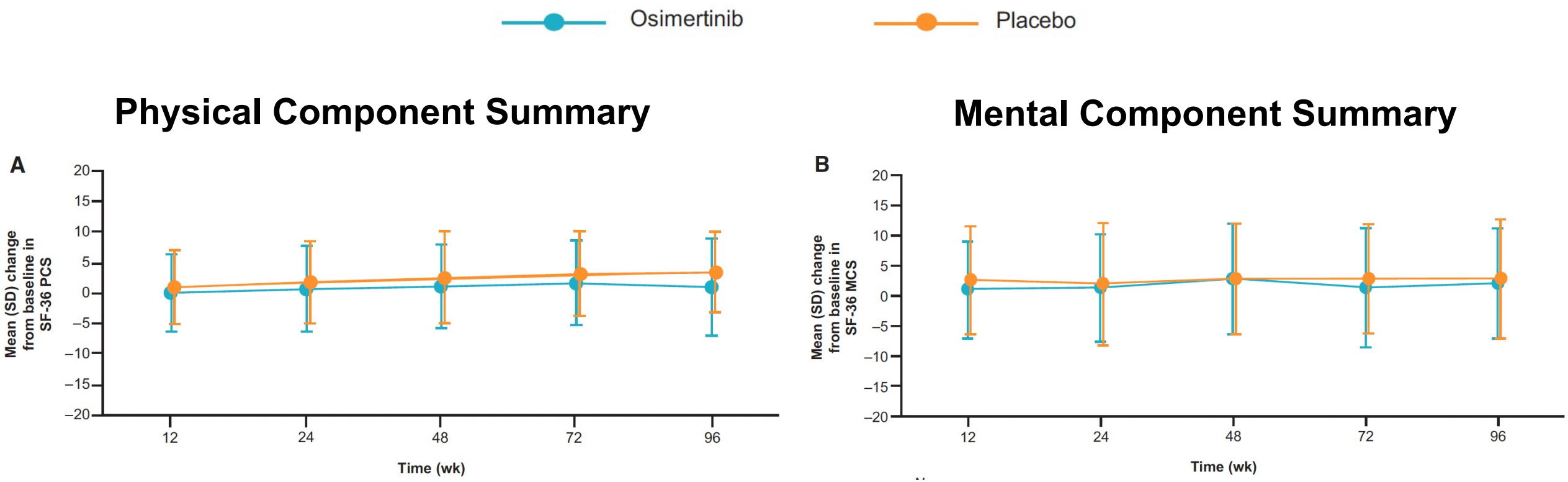
- **In patients with no push to treat, I have generally used single agent pembrolizumab**
- **Single agent cemiplimab or atezolizumab would be entirely appropriate**
- **Chemotherapy plus PD-(L)1 inhibition approaches would be options**
- **Chemotherapy plus PD-(L)1 inhibition and CTLA-4 inhibition would be an option**
- **Nivolumab and ipilimumab would be approved, but I would avoid in this setting**

Commentary – Edward B Garon, MD, MS

- **Patient presented with pleural effusion displacing the mediastinum**
- **Started carboplatin, pemetrexed and pembrolizumab**
- **Had an excellent response**
- **Stopped all therapy briefly during the initial COVID surge**
- **Eventually was willing to resume every six week dosing of pembrolizumab**

Appendix

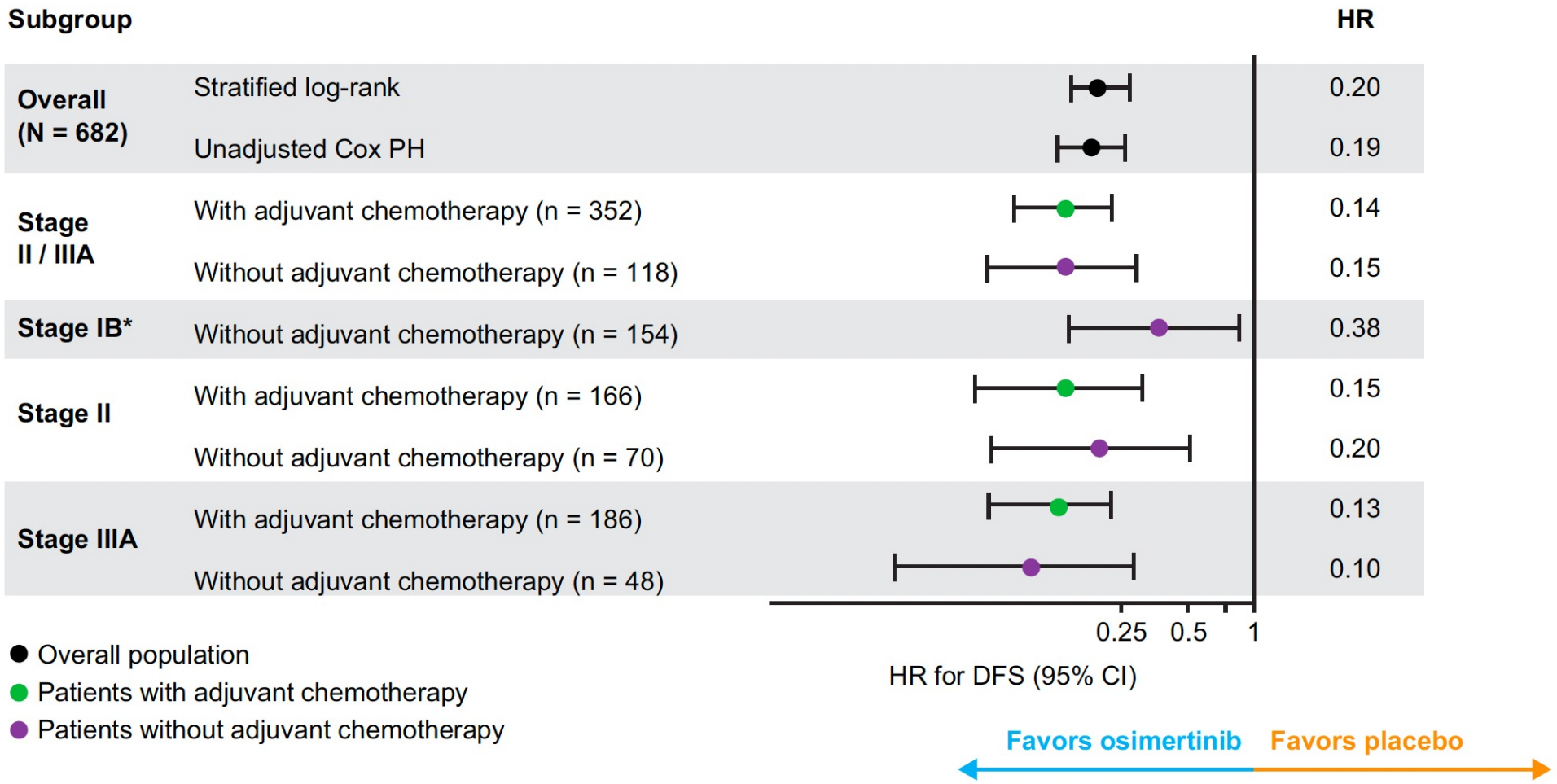
ADAURA: Health-Related Quality of Life Over Time



Majem M et al. *Clin Cancer Res* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

ADAURA: Updated DFS with Adjuvant Osimertinib for Patients Receiving and Not Receiving Adjuvant Chemotherapy — Subgroups



Wu YL et al. *J Thorac Oncol* 2022;17(3):423-33.

FDA Grants Accelerated Approval to Amivantamab-vmjw for Metastatic NSCLC

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."

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

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Mobocertinib for Metastatic NSCLC with EGFR Exon 20 Insertion Mutations

Press Release – September 15, 2021

"The Food and Drug Administration granted accelerated approval to mobocertinib 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.

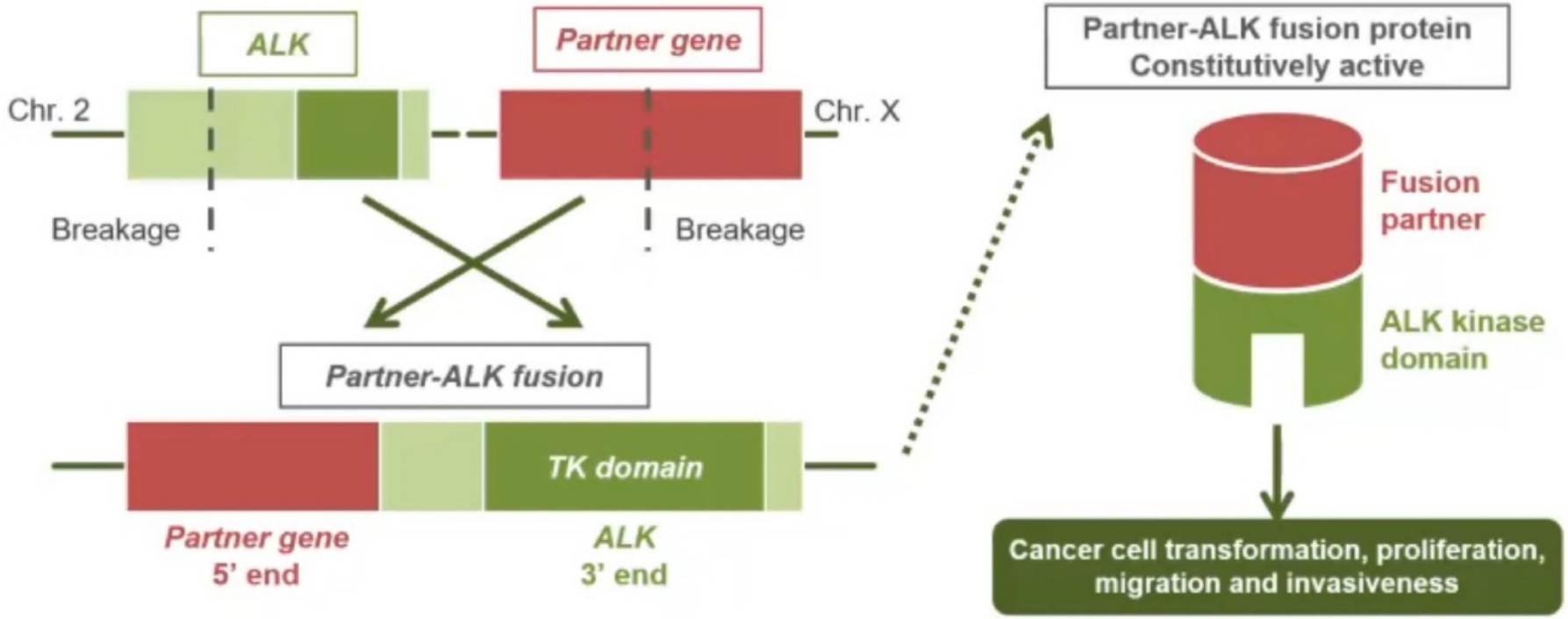
Today, the FDA also approved the Oncomine Dx Target Test as a companion diagnostic device to select patients with the above mutations for mobocertinib treatment.

Approval was based on Study 101, an international, non-randomized, open-label, multicohort clinical trial (NCT02716116) which included patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. Efficacy was evaluated in 114 patients whose disease had progressed on or after platinum-based chemotherapy. Patients received mobocertinib 160 mg orally daily until disease progression or intolerable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mobocertinib-metastatic-non-small-cell-lung-cancer-egfr-exon-20

Mechanism of *ALK* Fusions

AACR American Association for Cancer Research' ANNUAL MEETING 2022 New Orleans
APRIL 8-13 • #AACR22



Meric-Bernstam F et al. AACR 2022;Abstract CT032

Key Randomized Trials in Treatment-Naïve Advanced ALK-Rearranged NSCLC

Study	Intervention	Comparator	ORR	CNS ORR
PROFILE 1014	Crizotinib	Platinum/pemetrexed	74% vs 45%	—
PROFILE 1029	Crizotinib	Platinum/pemetrexed	88% vs 46%	—
ASCEND-4	Ceritinib	Platinum/pemetrexed	73% vs 27%	73% vs 27%
ALEX	Alectinib	Crizotinib	83% vs 76%	81% vs 50%
J-ALEX	Alectinib	Crizotinib	92% vs 79%	—
ALESIA	Alectinib	Crizotinib	91% vs 77%	—
ALTA-1L	Brigatinib	Crizotinib	71% vs 60%	78% vs 26%
CROWN	Lorlatinib	Crizotinib	76% vs 58%	82% vs 23%
eXalt3	Ensartinib	Crizotinib	75% vs 67%	64% vs 21%

Tan AC et al. *J Clin Oncol* 2022;40(6):611-25; Soria JC et al. *Lancet* 2017;389(10072):917-29; Peters S et al. *N Engl J Med* 2017;377(9):829-38; Camidge DR et al. *J Thorac Oncol* 2021;16(12):2091-108; Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29; Horn L et al. *JAMA Oncol* 2021;7(11):1617-25; Popat S et al. ESMO 2021;Abstract 1195P.

Key Randomized Trials in Treatment-Naïve Advanced ALK-Rearranged NSCLC (Continued)

Study	Intervention	Comparator	Median PFS	PFS Hazard ratio	OS Hazard ratio
PROFILE 1014	Crizotinib	Platinum/pemetrexed	11 vs 7 mo	0.45	0.76
PROFILE 1029	Crizotinib	Platinum/pemetrexed	11 vs 7 mo	0.40	0.90
ASCEND-4	Ceritinib	Platinum/pemetrexed	17 vs 8 mo	0.55	0.73
ALEX	Alectinib	Crizotinib	35 vs 11 mo	0.50	0.67
J-ALEX	Alectinib	Crizotinib	34 vs 10 mo	0.37	0.80
ALESIA	Alectinib	Crizotinib	NR v 11 mo	0.37	0.28
ALTA-1L	Brigatinib	Crizotinib	24 vs 11 mo	0.49	0.92
CROWN	Lorlatinib	Crizotinib	NR vs 9 mo	0.28	0.72
eXalt3	Ensartinib	Crizotinib	26 vs 13 mo	0.52	0.88

Tan AC et al. *J Clin Oncol* 2022;40(6):611-25; Soria JC et al. *Lancet* 2017;389(10072):917-29; Peters S et al. *N Engl J Med* 2017;377(9):829-38; Camidge DR et al. *J Thorac Oncol* 2021;16(12):2091-108; Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29; Horn L et al. *JAMA Oncol* 2021;7(11):1617-25; Popat S et al. ESMO 2021;Abstract 1195P.

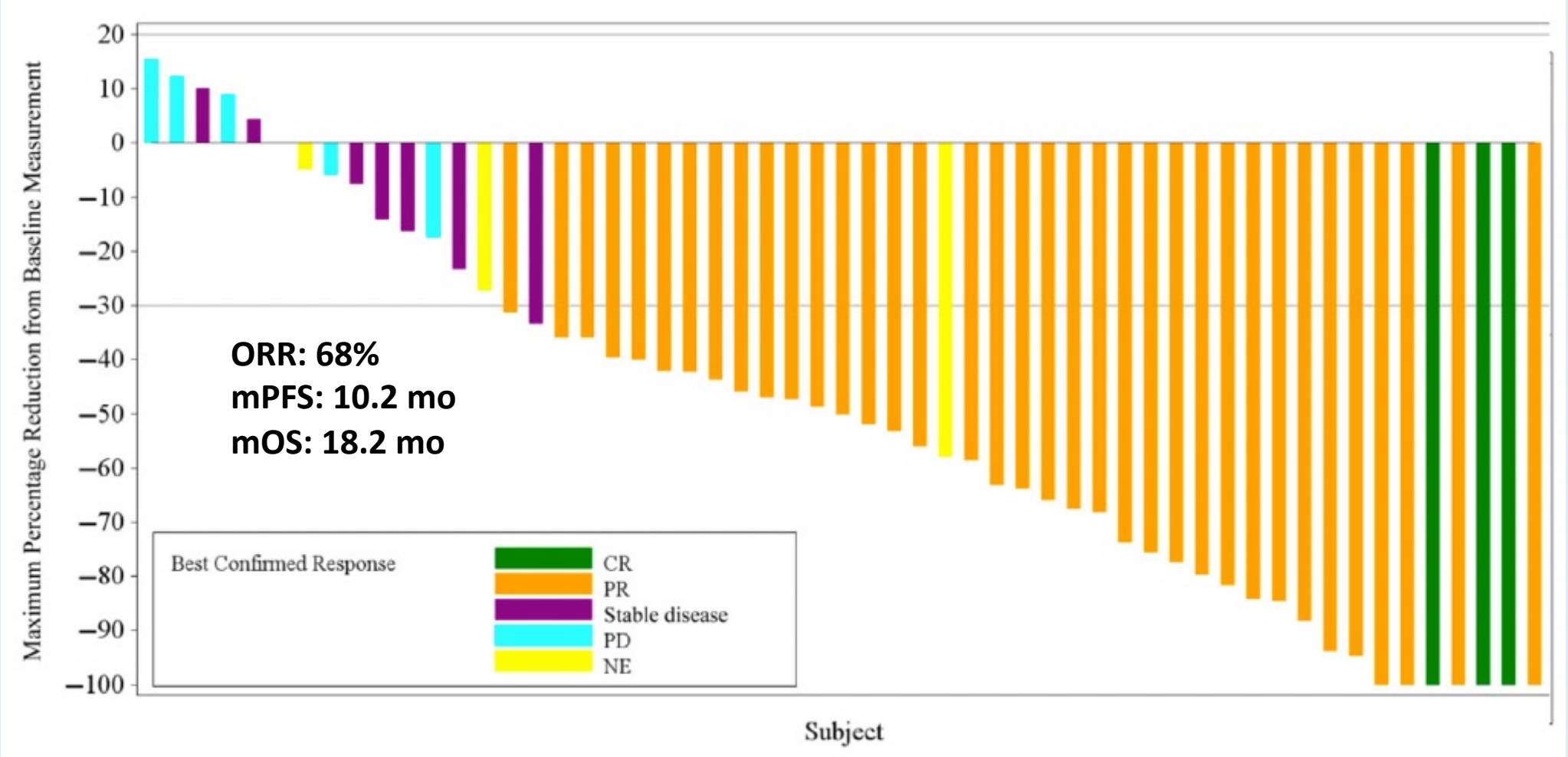
Ongoing Phase III Trials of Selpercatinib or Pralsetinib for NSCLC with RET Fusion

Trial identifier	Setting	Treatment arms
LIBRETTO-431 (NCT04194944)	Untreated Stage IIIB-IIIC or Stage IV nonsquamous NSCLC that is not suitable for radical surgery or radiation therapy	• Selpercatinib • Pemetrexed and platinum with or without pembrolizumab
LIBRETTO-432 (NCT04819100)	Stage IB, II or IIIA NSCLC after definitive locoregional therapy	• Selpercatinib • Placebo
AcceleRET-Lung (NCT04222972)	Locally advanced or metastatic NSCLC that has not been treated with systemic anticancer therapy for metastatic disease	• Pralsetinib • Platinum-based chemotherapy (with or without pembrolizumab)
NCT05170204	Unresectable Stage III NSCLC	Cohort A3 • Pralsetinib • Durvalumab

www.clinicaltrials.gov; Accessed March 2022.

Five-Year Update of a Phase II Study of Dabrafenib/Trametinib for Metastatic NSCLC with BRAF V600E Mutation

Pretreated Disease (N = 57)

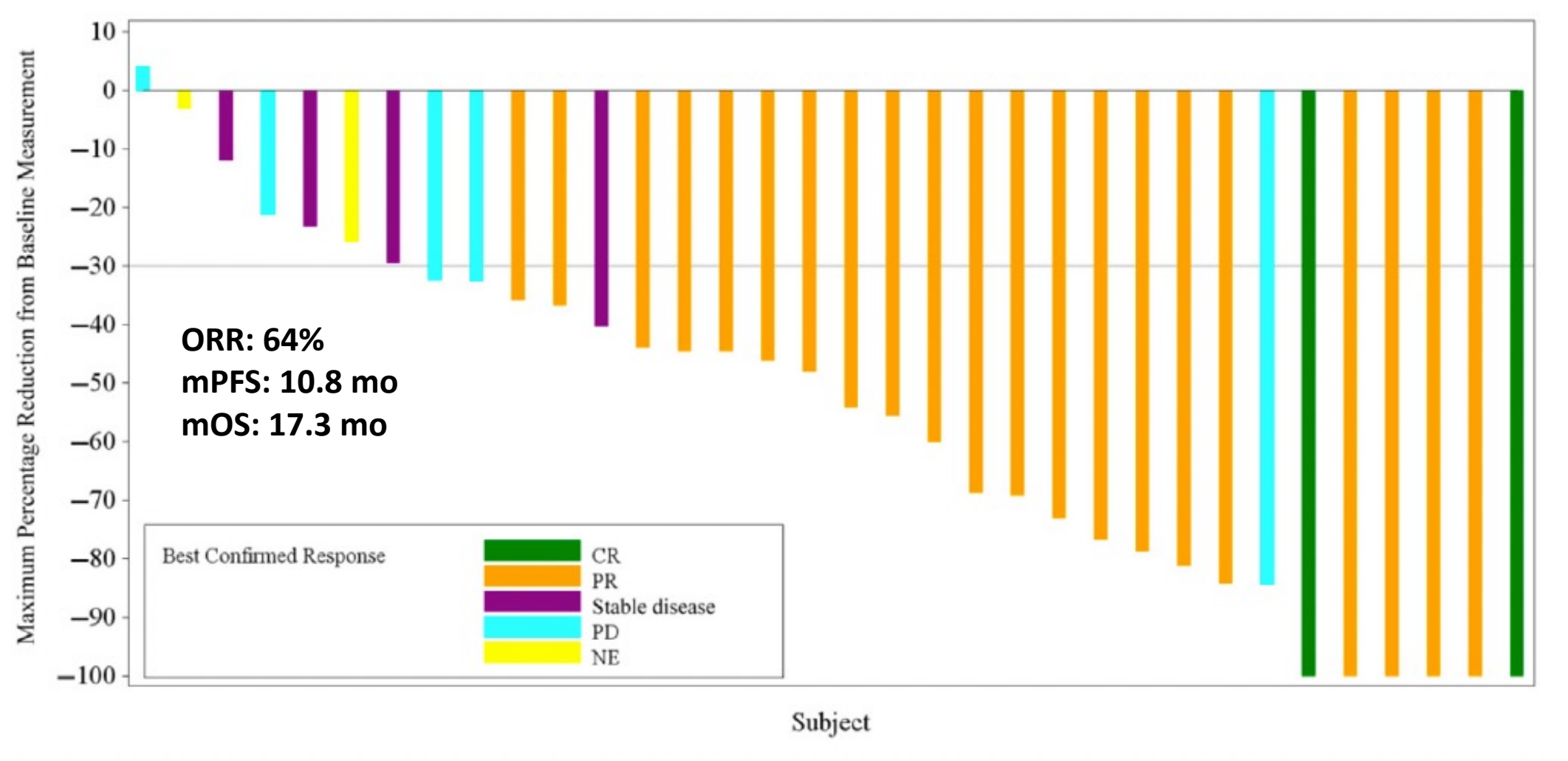


Planchard D et al. *J Thorac Oncol* 2022;17(1):103-15.

RTP RESEARCH TO PRACTICE

Five-Year Update of a Phase II Study of Dabrafenib/Trametinib for Metastatic NSCLC with BRAF V600E Mutation

Treatment-Naïve Disease (N = 36)



Planchard D et al. *J Thorac Oncol* 2022;17(1):103-15.

Key Trials of ROS1 Tyrosine Kinase Inhibitors (TKIs) for TKI-Naïve NSCLC with ROS1 Fusions

ROS1 TKI	Study	Phase	ORR	Median DoR	Median PFS	Intracranial ORR
Crizotinib	PROFILE 1001	Ib	38/53 (72%)	25 mo	19 mo	—
	OxOnc	II	91/127 (72%)	20 mo	16 mo	—
	EUCROSS	II	21/30 (70%)	19 mo	20 mo	—
	AcSe	II	35/36 (69%)	—	6 mo	—
	METROS	II	17/26 (65%)	21 mo	23 mo	33%
Entrectinib	Drilon et al	I/II	41/53 (77%)	25 mo	19 mo	55%
Ceritinib	Lim et al	II	20/30 (67%)	21 mo	19 mo	29%
Brigatinib	Gettinger et al	I	1/1 (100%)	—	—	—
Lorlatinib	Shaw et al	I/II	13/21 (62%)	25 mo	21 mo	64%
Repotrectinib	Cho et al	I/II	10/11 (91%)	—	—	100%
Taletrectinib	Fujiwara et al	I	6/9 (67%)	—	—	—

Drilon A et al. *Nat Rev Clin Oncol* 2021;18(1):35-55.

FDA Grants Accelerated Approval to Sotorasib for NSCLC with KRAS G12C Mutation

Press Release – May 28, 2021

"The Food and Drug Administration granted accelerated approval to sotorasib, a RAS GTPase family inhibitor, for adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

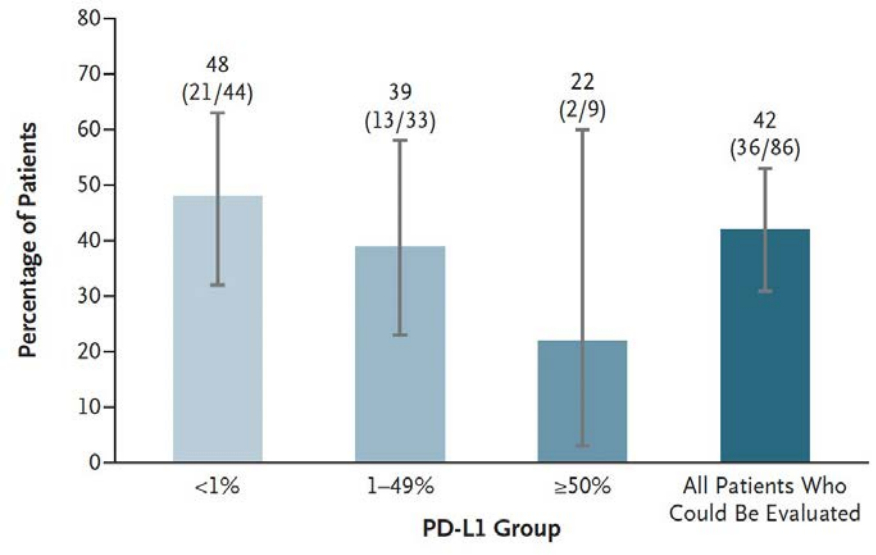
FDA also approved the QIAGEN therascreen® KRAS RGQ PCR kit (tissue) and the Guardant360® CDx (plasma) as companion diagnostics for sotorasib. If no mutation is detected in a plasma specimen, the tumor tissue should be tested.

Approval was based on CodeBreaK 100, a multicenter, single-arm, open label clinical trial (NCT03600883) which included patients with locally advanced or metastatic NSCLC with KRAS G12C mutations. Efficacy was evaluated in 124 patients whose disease had progressed on or after at least one prior systemic therapy. Patients received sotorasib 960 mg orally daily until disease progression or unacceptable toxicity."

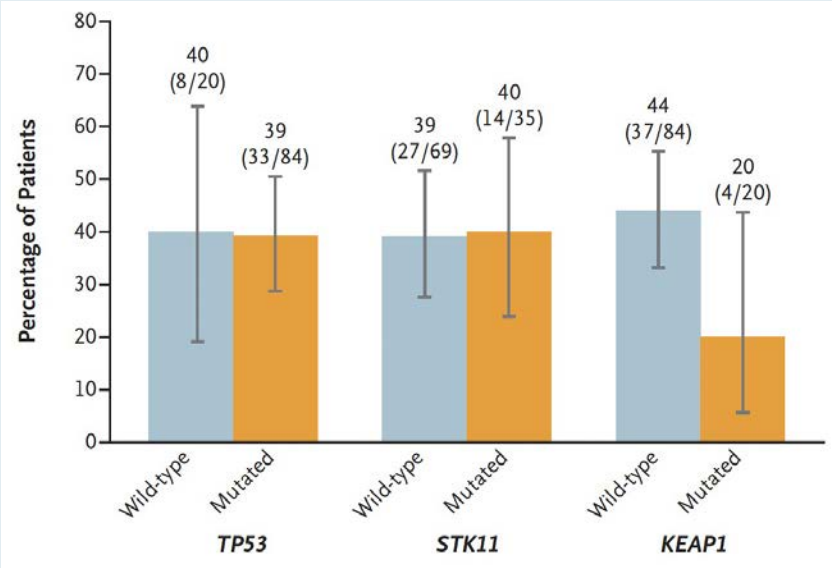
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sotorasib-kras-g12c-mutated-nsclc

CodeBreaK 100: Exploratory Biomarker Analyses

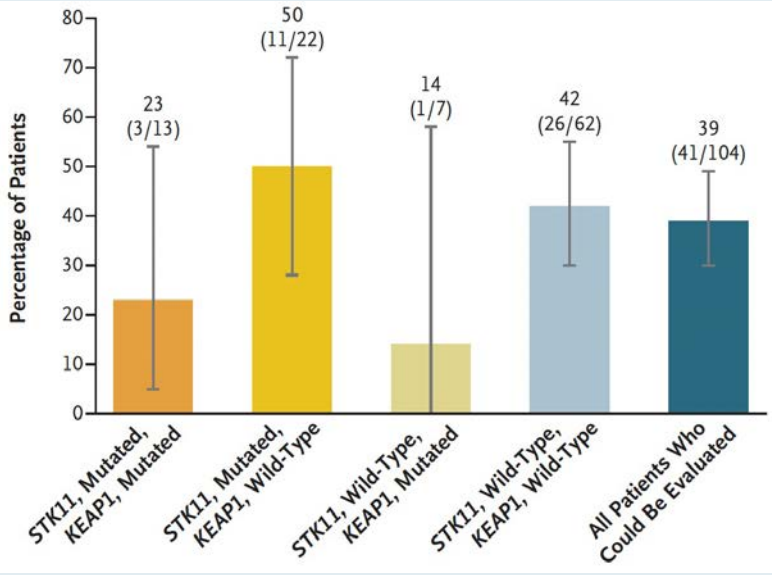
Response According to PD-L1 Expression Level



Response According to Co-occurring Mutations in TP53, STK11 and KEAP1



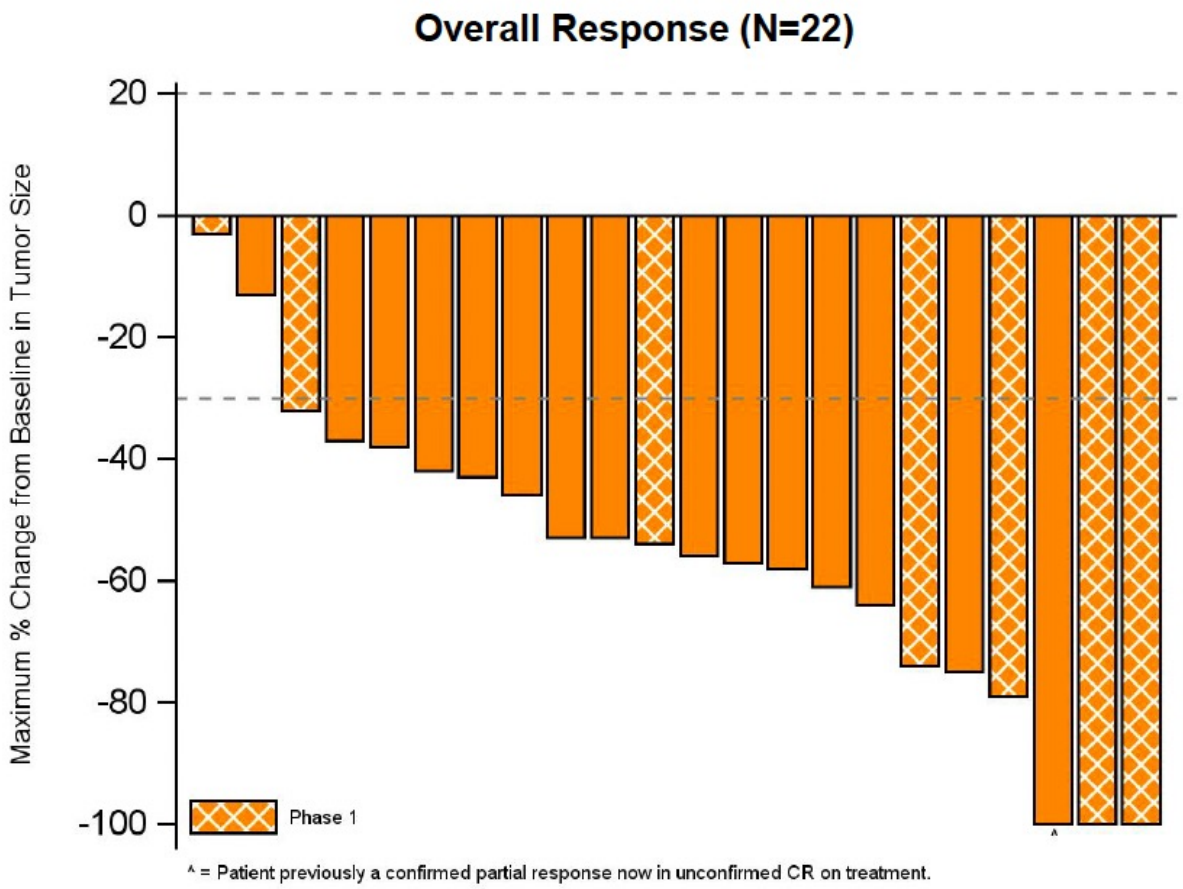
Response According to Mutational Status in Both STK11 and KEAP1



Skoulidis F et al. *N Engl J Med* 2021;384(25):2371-81.

RTP RESEARCH TO PRACTICE

TRIDENT-1: Clinical Activity of Repotrectinib in TKI-Naïve Advanced NSCLC with ROS1 Fusions



	Phase 2 N=15	Phase 1+2 N=22
Confirmed ORR, % (95% CI)	93% (68–100)	91% (71–99)

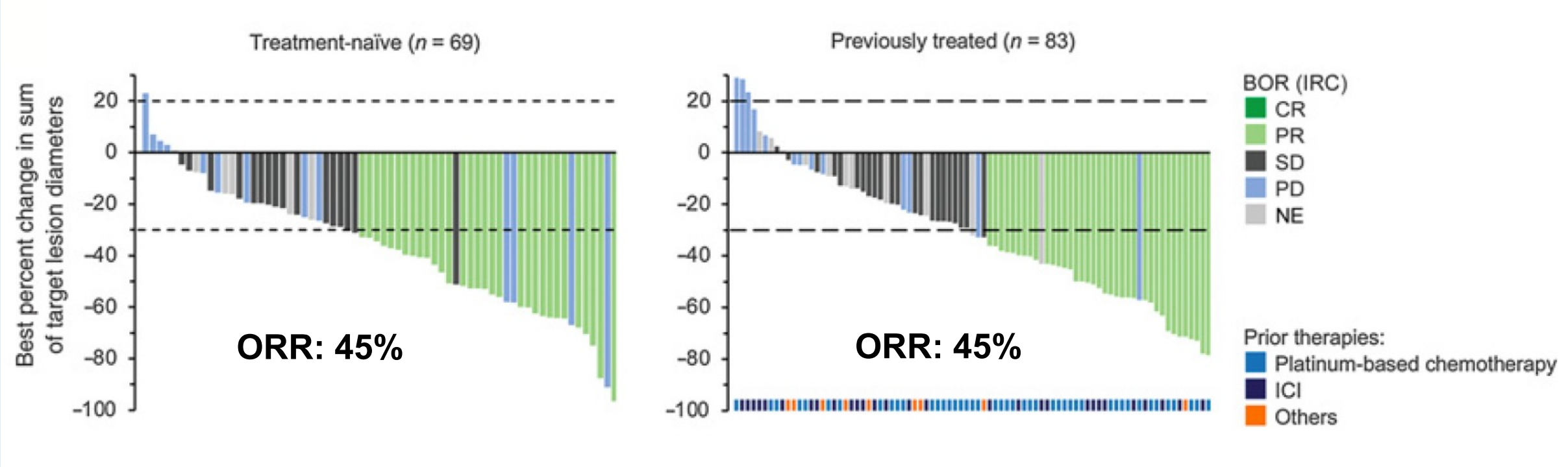
N=22 patients with baseline and at least two post baseline scans

- *N=15 Phase 2 patients*
- *N=7 Phase 1 patients treated at or above the Phase 2 recommended dose*

As of 31 December 2020, the 16th patient in Phase 2 has an unconfirmed PR and is on treatment awaiting a second post-baseline confirmatory scan.

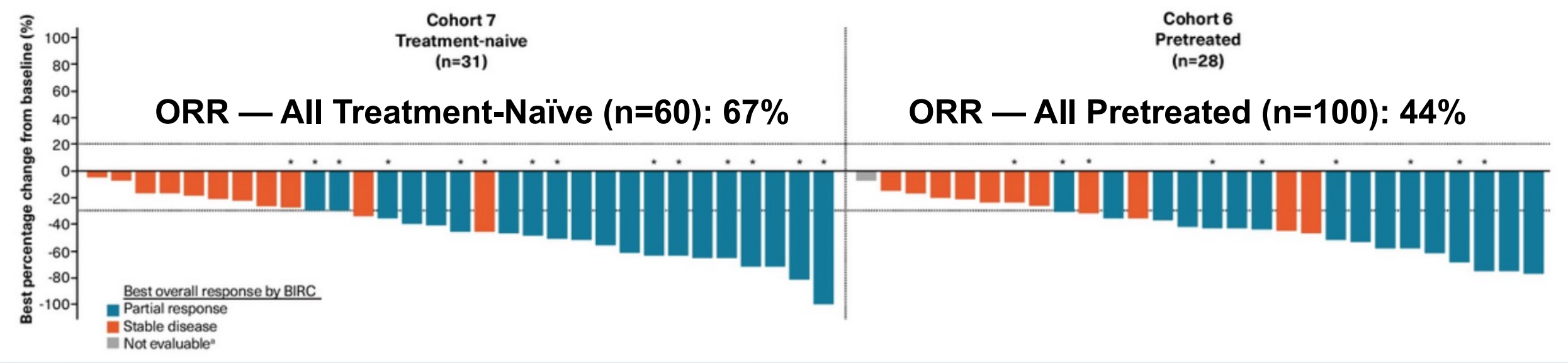
Cho BC et al. WCLC 2020;Abstract 3255.

VISION: Tepotinib in Advanced NSCLC with MET Exon 14 Skipping Mutations



Le X et al. *Clin Cancer Res* 2022;28(6):1117-26.

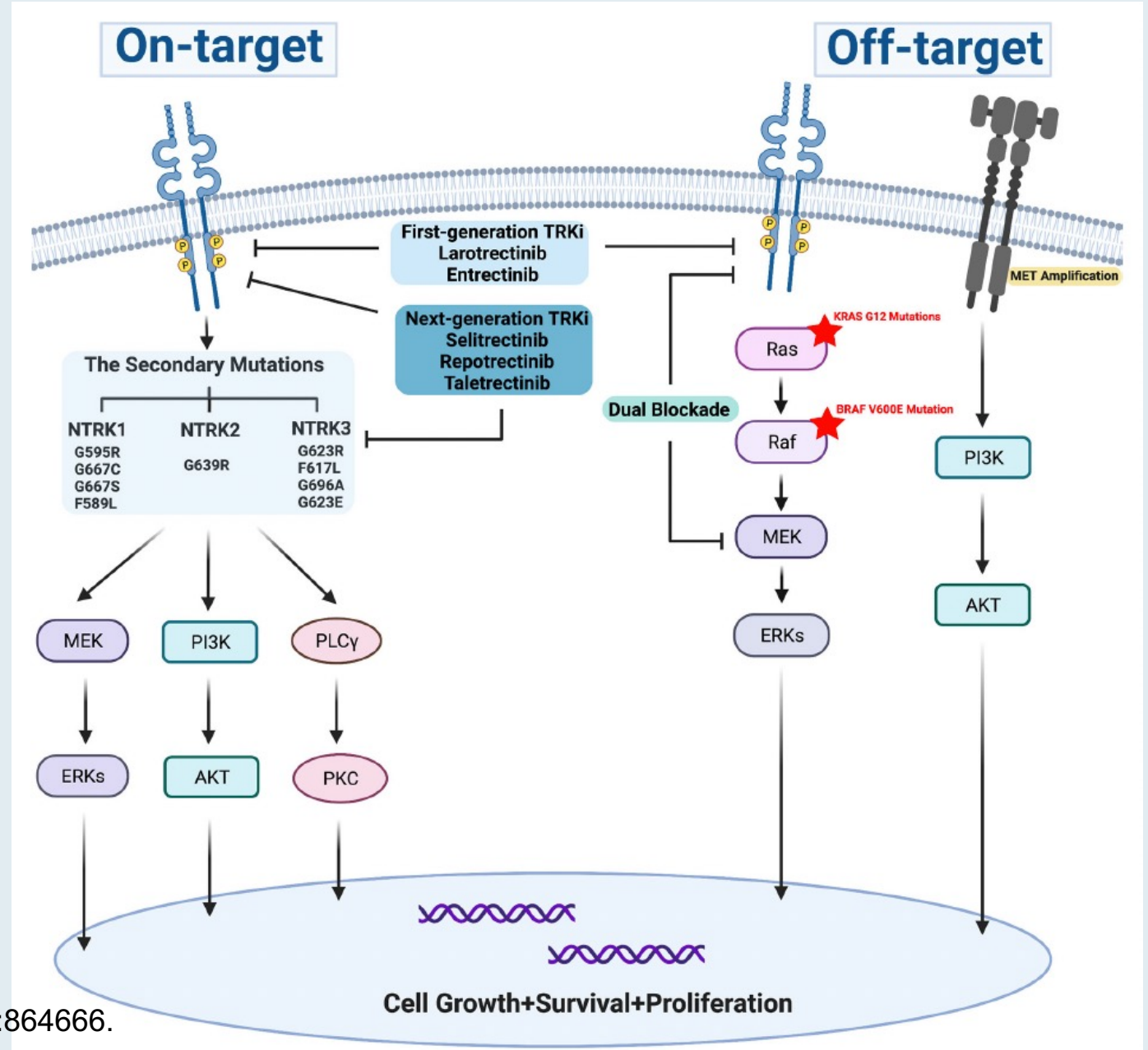
GEOMETRY mono-1: Capmatinib Overall Response Rates (Cohorts 7 and 6)



Wolf J et al. ASCO 2021;Abstract 9020.

RTP RESEARCH TO PRACTICE

Mechanism of Action and Resistance to First-Generation TRK TKIs



Liu F et al. *Front Oncol* 2022;12:864666.

Efficacy of First-Generation TRK Inhibitors for Locally Advanced or Metastatic Solid Cancers Harboring NTRK Rearrangements

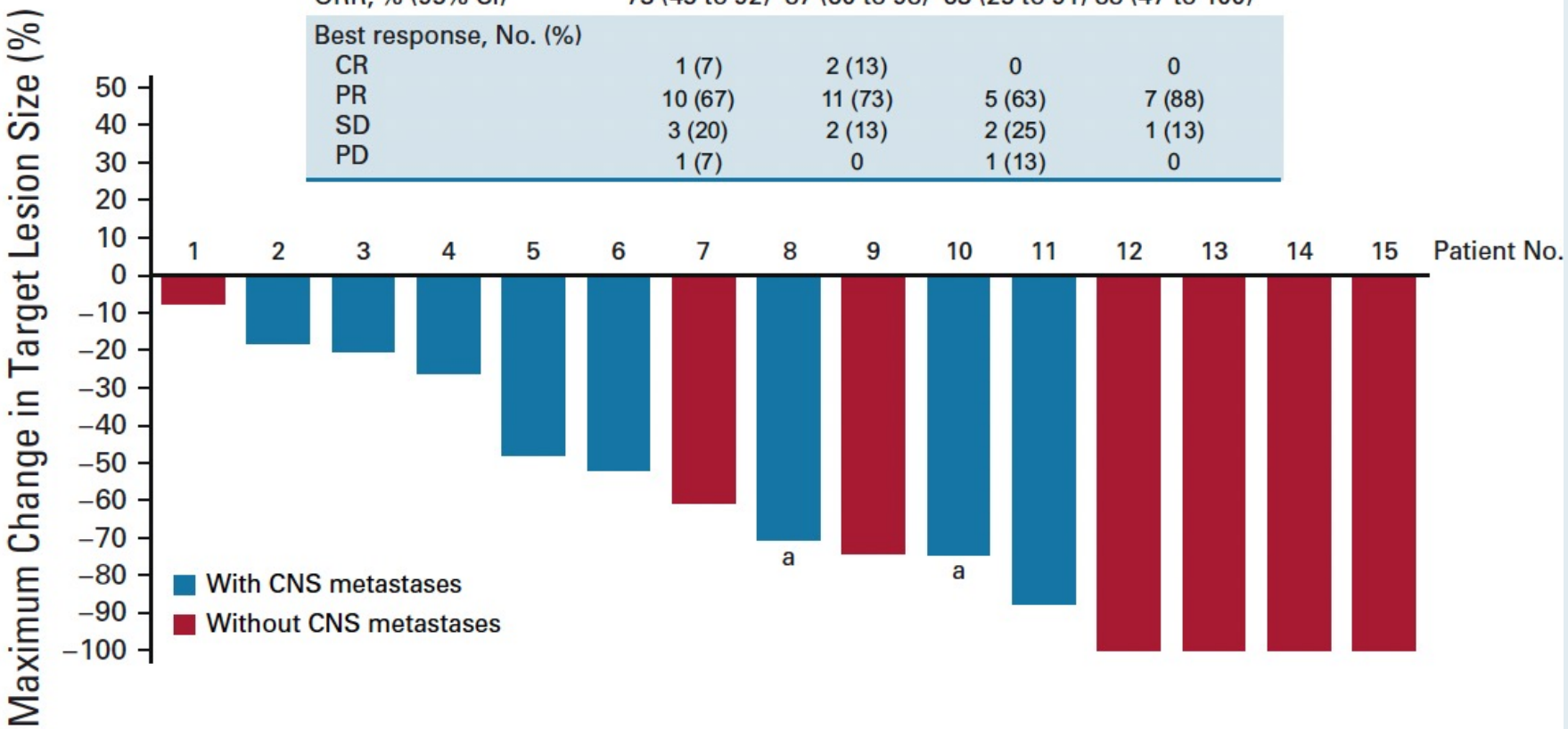
	Overall Population				NSCLC	
TRK inhibitor	**N**	**ORR**	**CNS ORR**	**Median PFS**	**N**	**ORR**
Larotrectinib	159	79%	75%	28.3 mo	12	75%
Entrectinib	54	57%	50%	11.2 mo	10	70%

Liu F et al. *Front Oncol* 2022;12:864666.

RTP RESEARCH TO PRACTICE

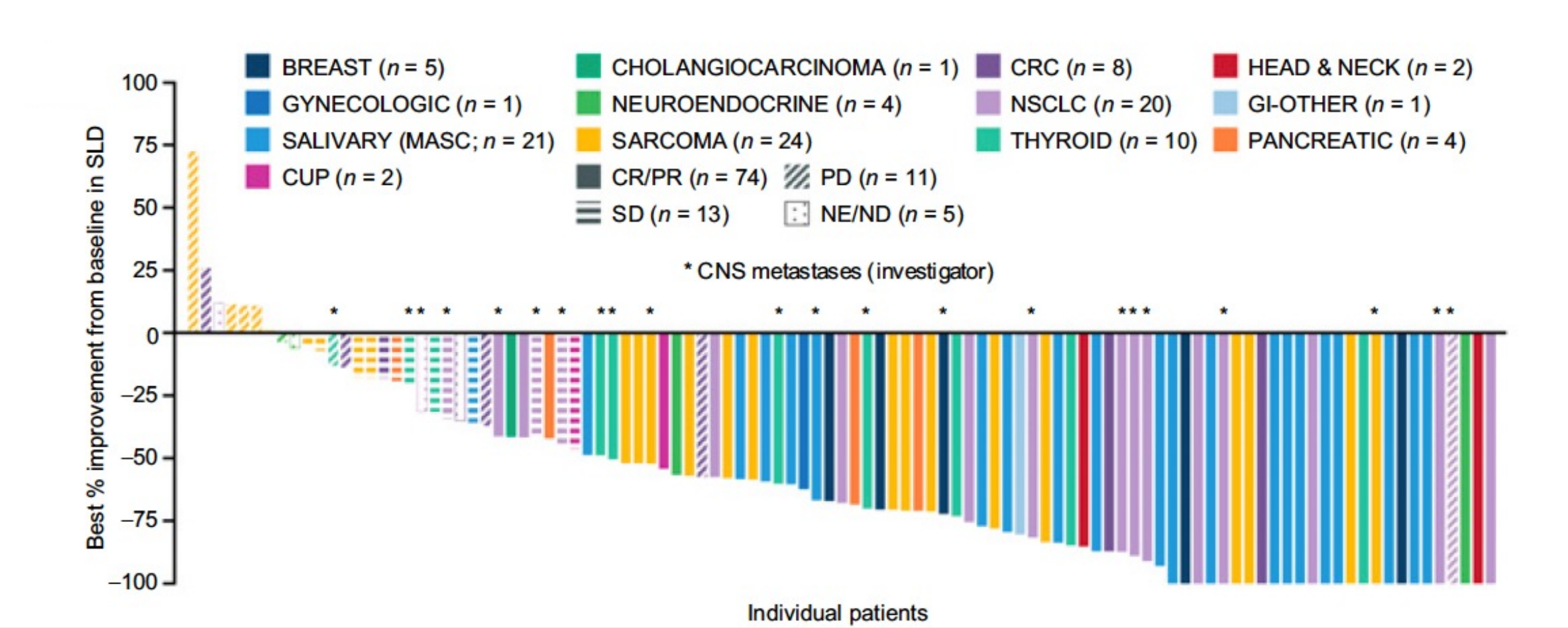
Efficacy and Safety of Larotrectinib in Patients with TRK-Positive Advanced Lung Cancer

	All Patients (N = 20)		Patients With CNS Metastases (n = 10)	
	INV	IRC	INV	IRC
Evaluable patients, No.	15	15	8	8
ORR, % (95% CI)	73 (45 to 92)	87 (60 to 98)	63 (25 to 91)	88 (47 to 100)
Best response, No. (%)				
CR	1 (7)	2 (13)	0	0
PR	10 (67)	11 (73)	5 (63)	7 (88)
SD	3 (20)	2 (13)	2 (25)	1 (13)
PD	1 (7)	0	1 (13)	0



Drilon A et al. *JCO Precis Oncol* 2022;6:e2100418.

Updated Integrated Analysis of ALKA-372-001, STARTRK-1 and STARTRK-2: Entrectinib for Solid Tumors with NTRK Fusion



Demetri GD et al. *Clin Cancer Res* 2022;28(7):1302-12.

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.

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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: Safety Summary

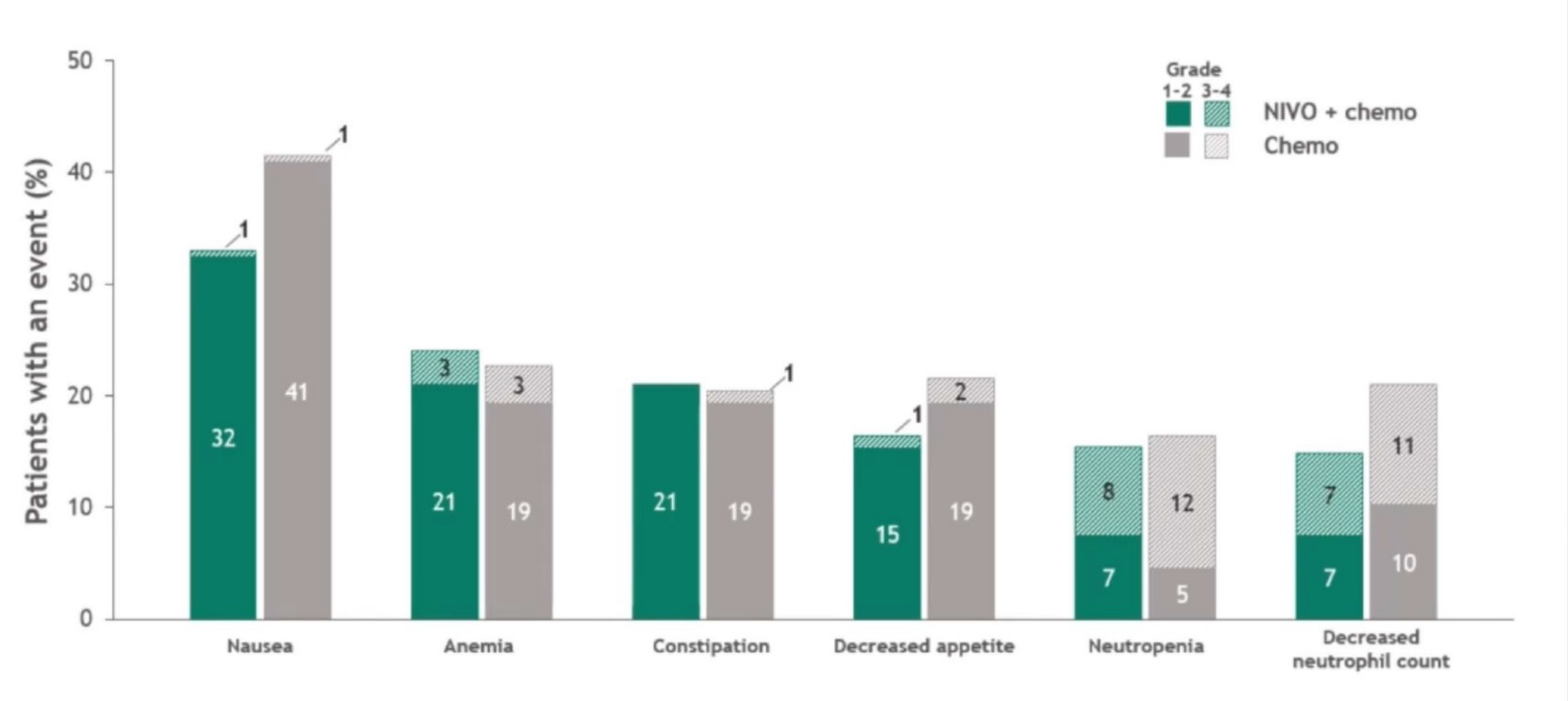
	Atezolizumab group (n=495)	Best supportive care group (n=495)
Adverse event		
Any grade	459 (93%)	350 (71%)
Grade 3–4	108 (22%)	57 (12%)
Serious	87 (18%)	42 (8%)
Grade 5	8 (2%)*	3 (1%)†
Led to dose interruption of atezolizumab	142 (29%)	..
Led to atezolizumab discontinuation	90 (18%)	..
Immune-mediated 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: Treatment-Related Adverse Events in ≥15% of Patients



Forde PM et al. AACR 2021;Abstract CT003.

What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Hepatobiliary Cancers

Thursday, April 28, 2022
8:20 PM – 9:20 PM PT

Faculty

Richard S Finn, MD
Amanda K Wagner, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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