Transforming Oncology Care
Through Medically Integrated Collaboration

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Optimizing Patient Outcomes in EGFR and NSCLC Sequencing

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OBJECTIVES

1. Analyze clinical evidence of front-line treatment options for advanced/metastatic Epidermal Growth Factor Receptor (EGFR)-mutant Non-Small Cell Lung Cancer (NSCLC).

2. Compare efficacy, toxicity, and administration of first-line treatments for EGFR-mutant NSCLC and how this informs shared decision making with the patient.

3. Examine subsequent therapy options following progression after front-line treatment and the sequencing of additional therapies.

4. Describe best practices for molecular testing and EMR integration to identify driver mutations in NSCLC patients.

DISCLOSURES

The following relevant financial relationships from the past 24 months have been identified and disclosed for the following faculty and planners of this CE activity:

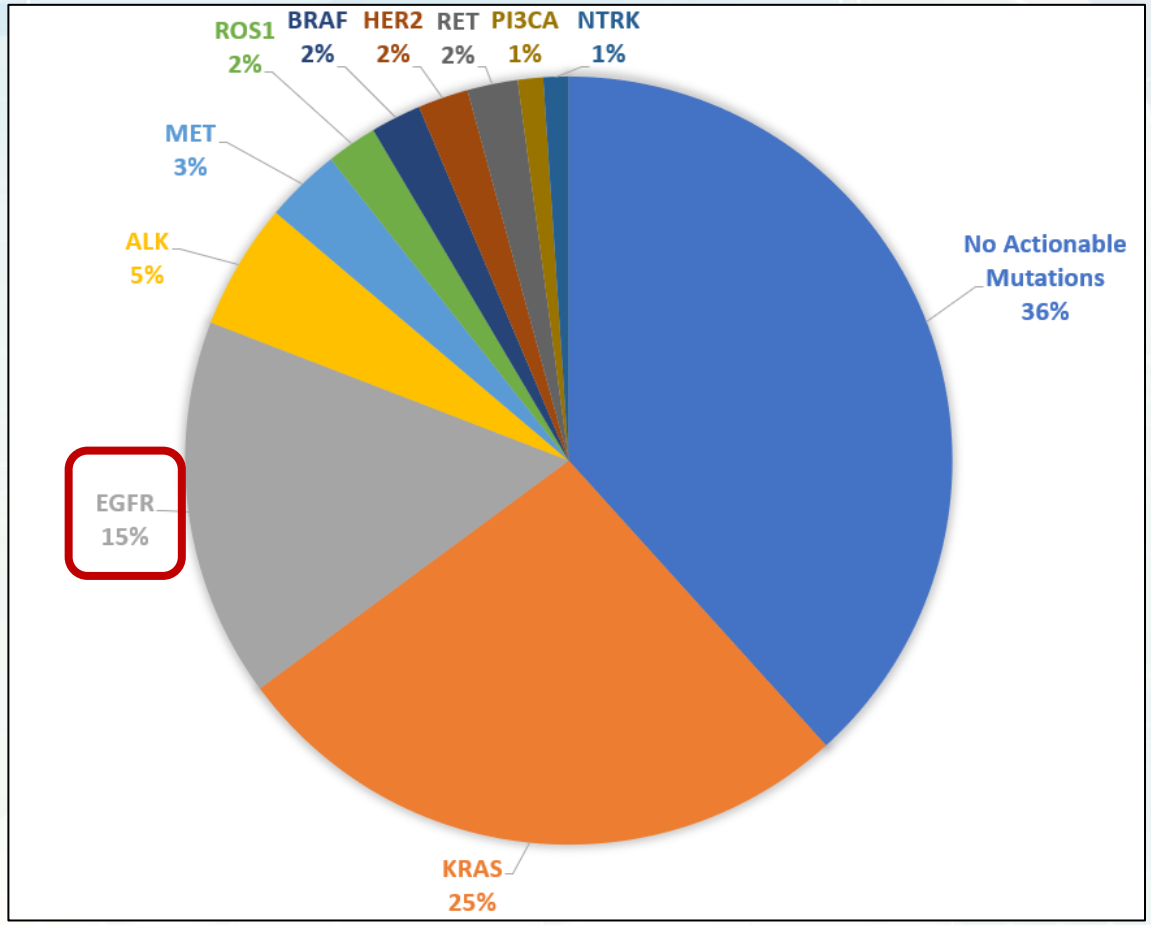
- Kevin Chen, PharmD, MS, BCOP, CPP
  - Advisory boards member for Johnson & Johnson, Pfizer, Bristol Myers Squibb, Amgen, Daiichi Sankyo
  - Contracted Research for Eli Lilly and Company

No relevant financial relationships from the past 24 months have been identified for the following planners of this CE activity:

- Tahsin Imam, PharmD

Background

- Lung cancer is the leading cause of cancer-related deaths
  - 1/6 deaths in light/non-smokers
- EGFR mutations are common
  - Younger
  - Female
  - East-Asian
  - Adenocarcinoma
  - Non-smokers
- Lung cancer screening is difficult



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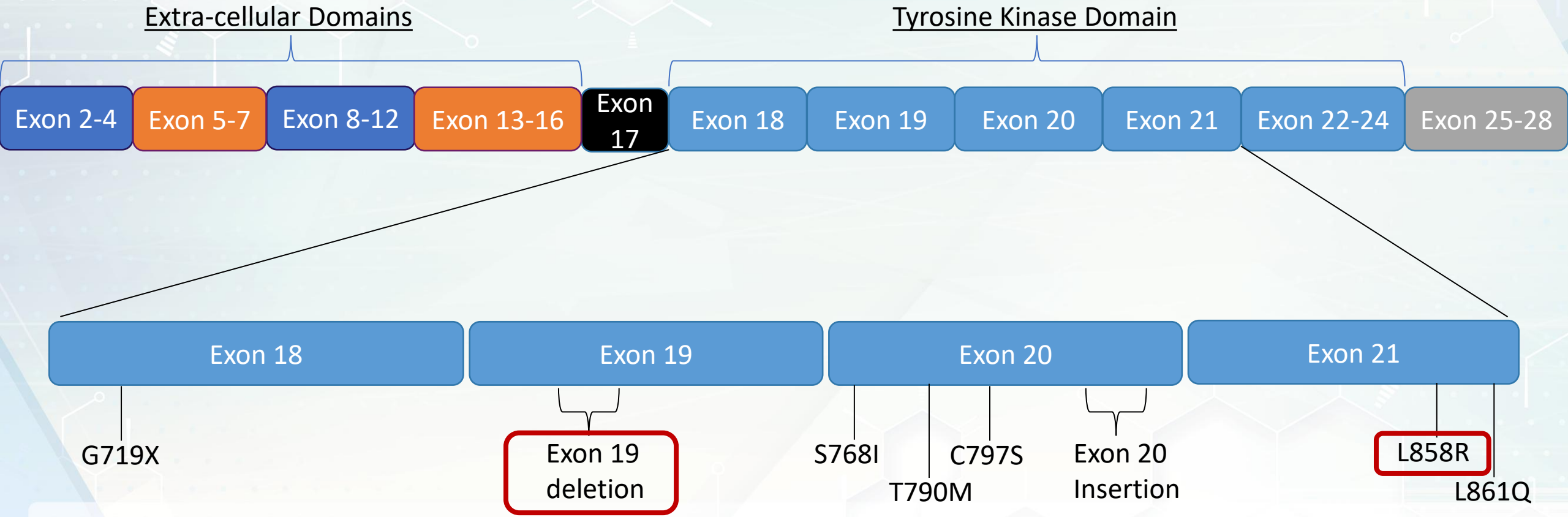
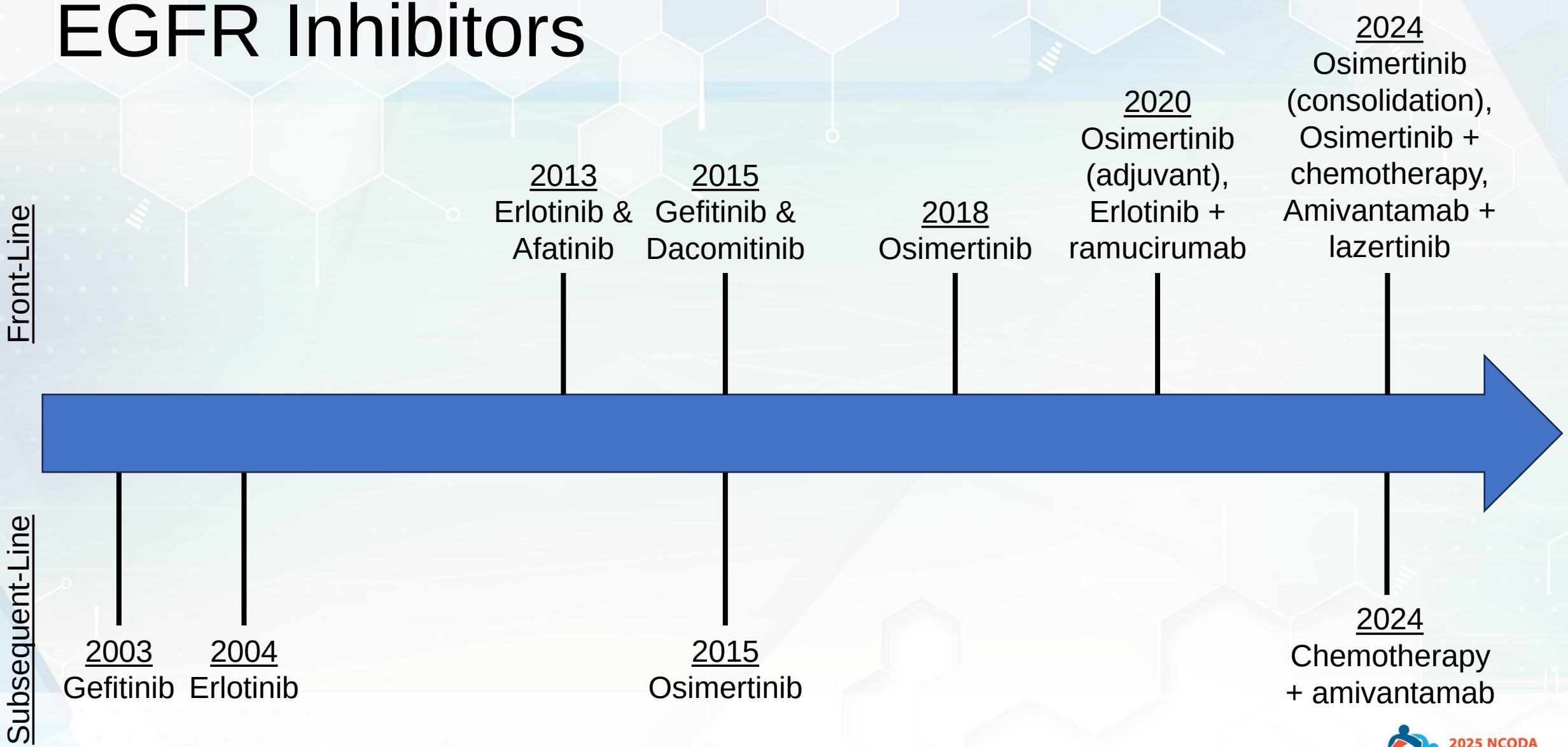
Seigel R, et al. CA Cancer J Clin. 2024;74(1):12-49; Pakkala S, Ramalingam SS. JCI Insight. 2018;3(15):e120858; Zhang YL, et al. Oncotarget. 2016;7(48):78985-78993.

EGFR Mutations



Robichaux, JP, et al. *Nature.* 2021;597(7878):732-737; Reiter JL, et al. *Genomics.* 2001;71(1):1-20.

EGFR Inhibitors



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Patient Case

- SH is a 49-year-old never-smoking female with newly-diagnosed NSCLC.
- PET/MRI show avid lesions in her right lower lobe, mediastinal lymph nodes, liver, left iliac crest, and right temporal lobe.
- Comprehensive molecular testing revealed an EGFR exon19 deletion and TP53 loss-of-function mutation.
- She presents to her medical oncologist to discuss first-line treatment options for her cancer.

QUESTION 1

What is your preferred front-line treatment regimen for patients with metastatic classically activating EGFR-mutant NSCLC?

A) Osimertinib monotherapy

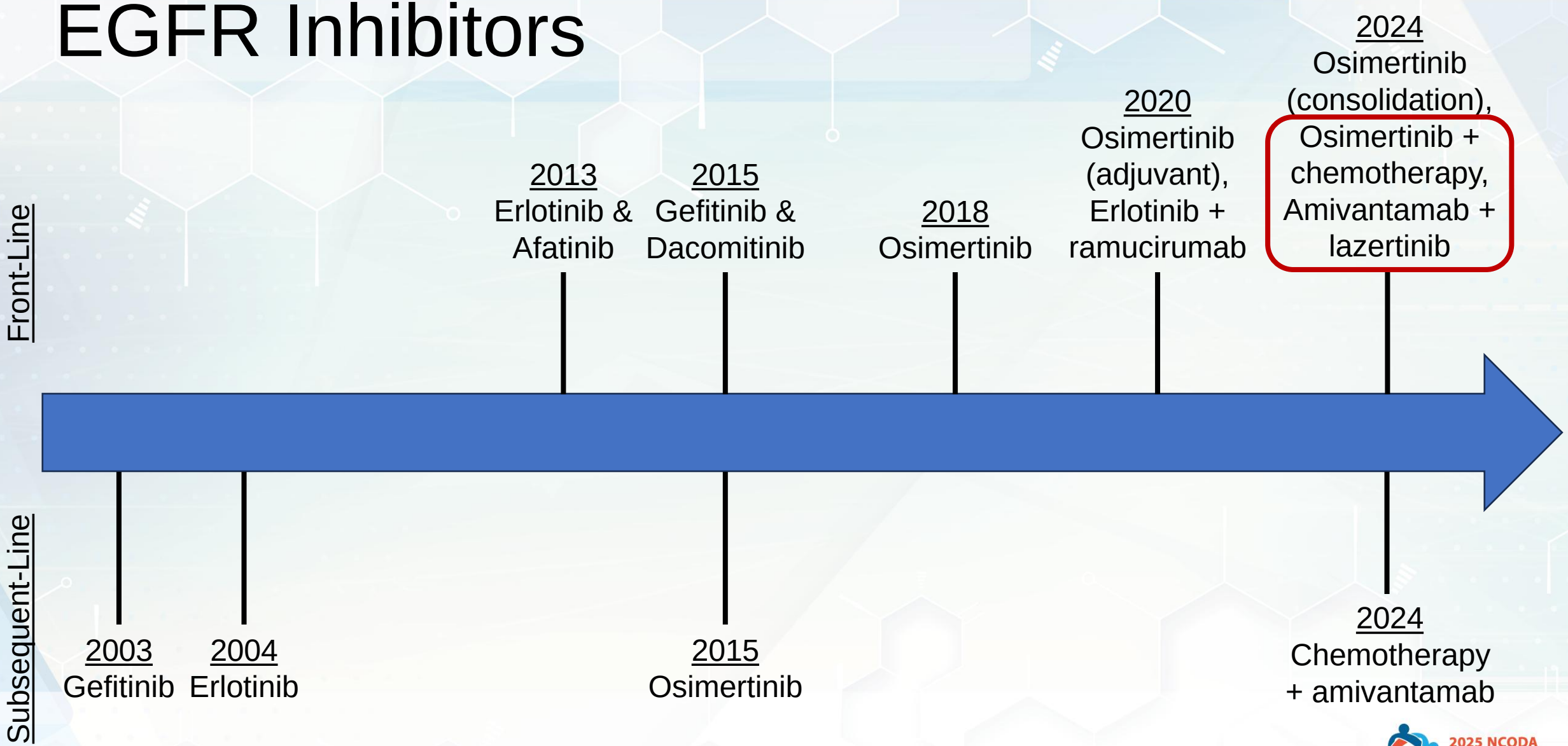
B) Osimertinib + chemotherapy

C) Amivantamab + lazertinib

D) Other

Front-Line Treatments

EGFR Inhibitors



FLAURA2 Design

Inclusion Criteria

- Locally advanced or metastatic NSCLC
- Treatment naïve
- EGFR exon19del or L858R
- WHO PS 0-1

Stratified

- EGFR testing (central vs local)
- Asian race
- WHO PS

Randomized

1 → **Chemo* + Osi 80mg PO daily (n=279)**

1 → **Osimertinib 80mg PO daily (n=278)**

Primary Endpoint

- PFS by BICR

Secondary Endpoints

- Overall survival
- ORR
- Duration of response
- Intracranial PFS
- Safety

*Chemotherapy Dosing (in 21d cycles)

Cisplatin: 75mg/m2 IV on D1 for 4 cycles

OR

Carboplatin: AUC 5 IV on D1 for 4 cycles

AND

Pemetrexed: 500mg/m2 IV on D1 until disease progression

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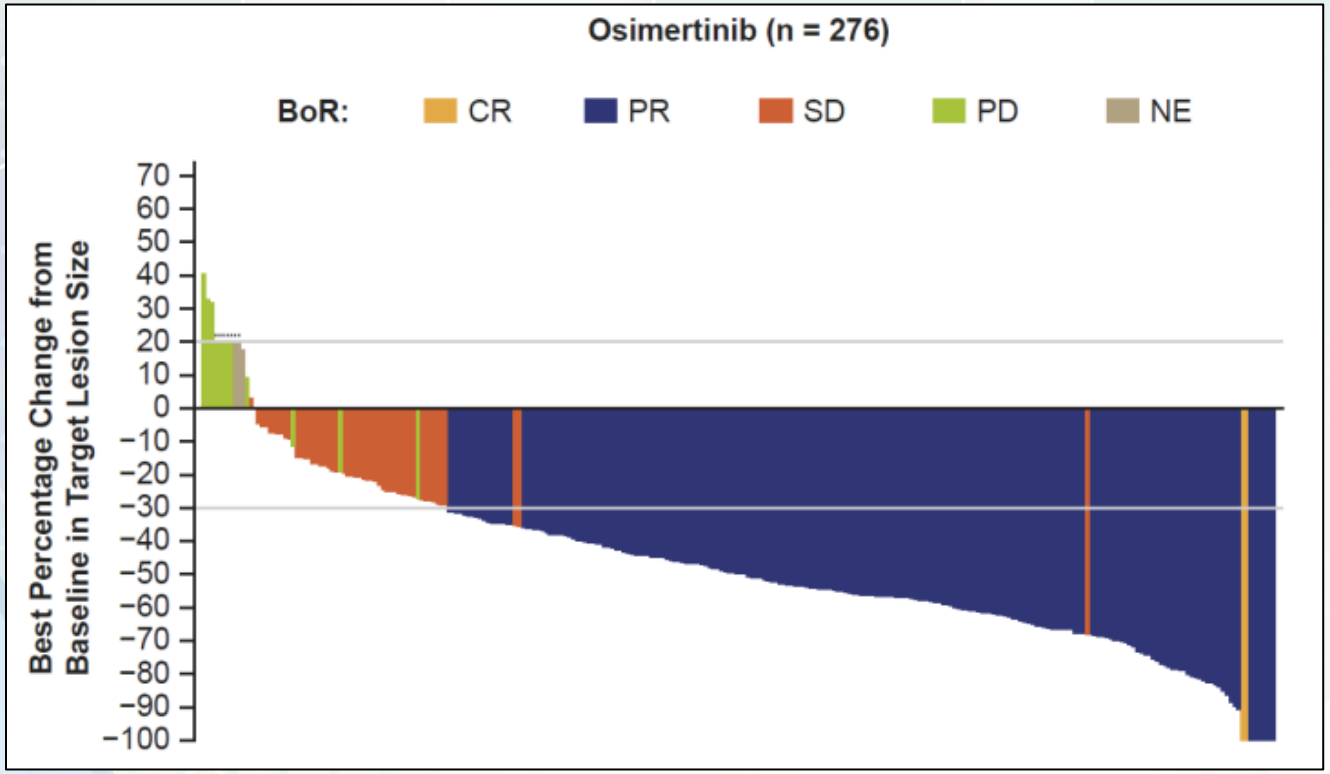
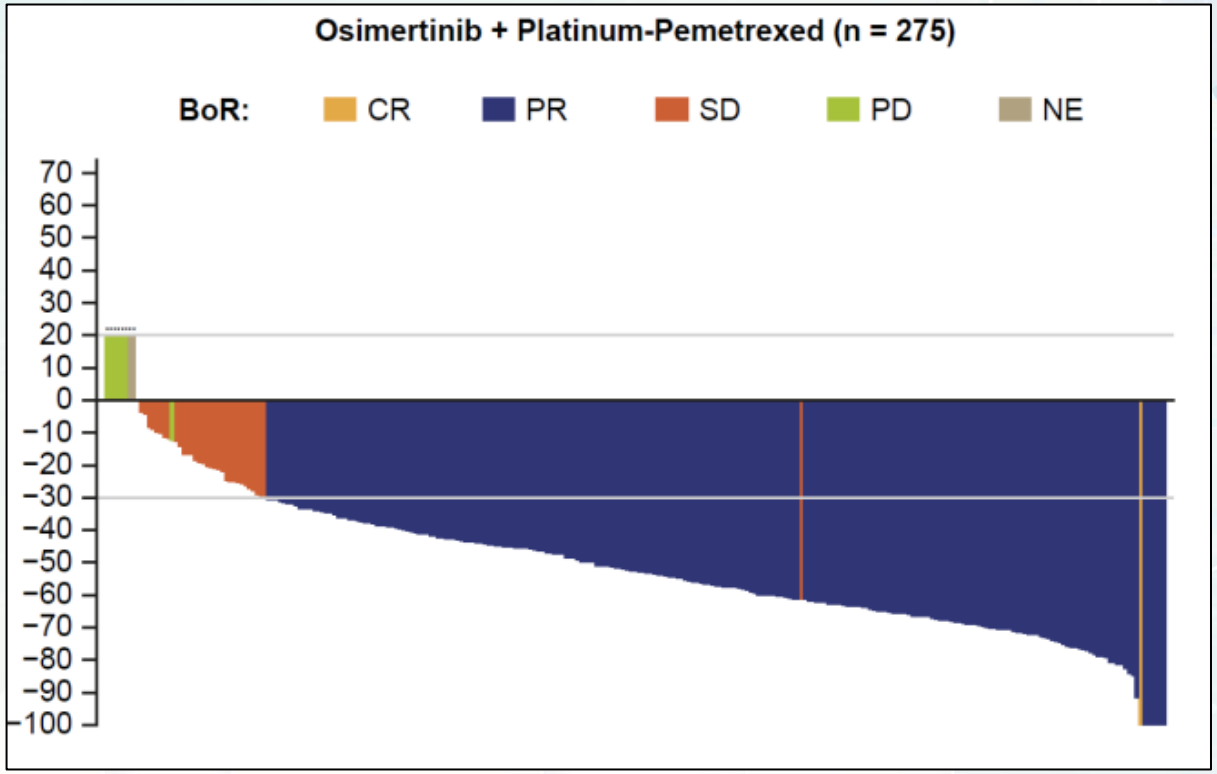
Planchard D,Y, et al. N Engl J Med. 2023;389(21):1935-1948.

FLAURA2 Efficacy





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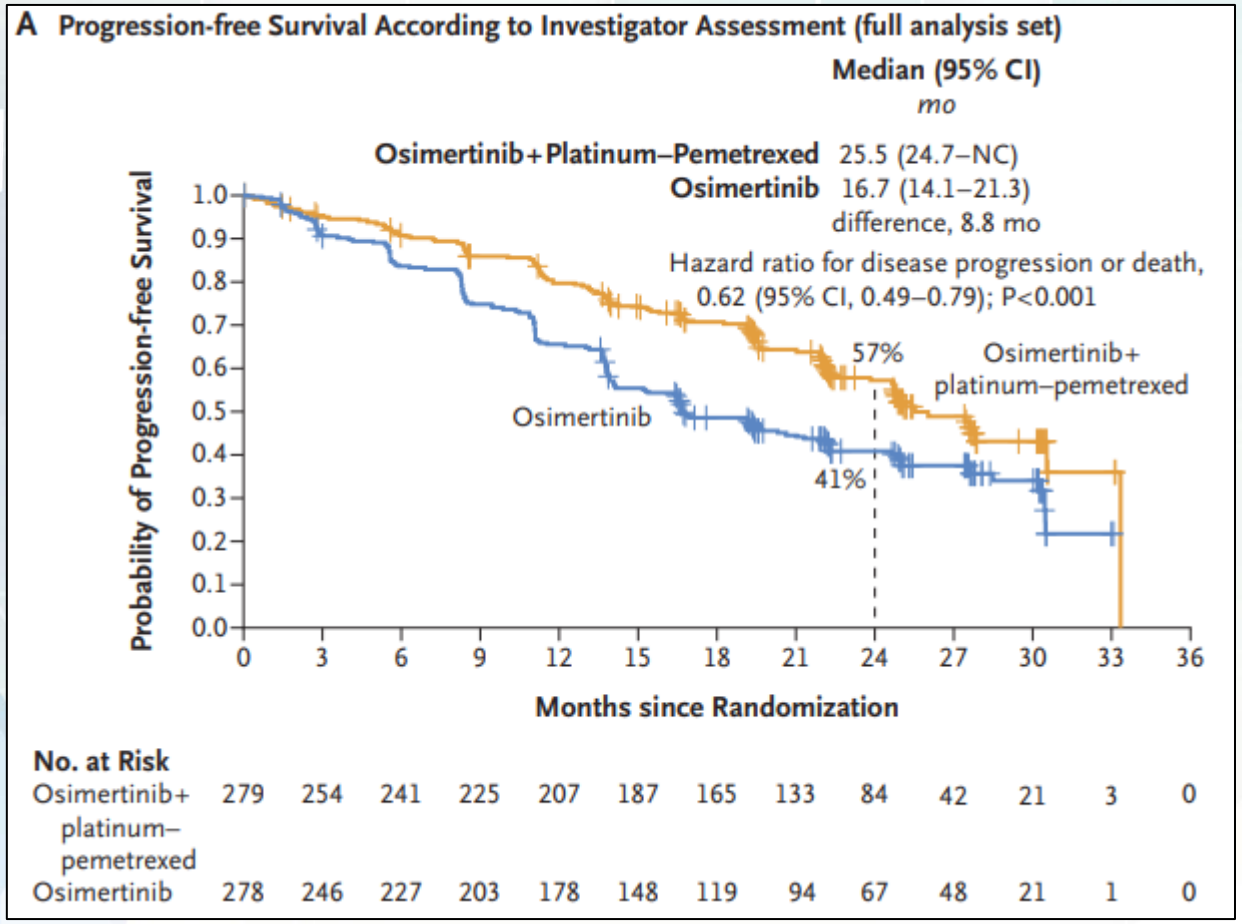
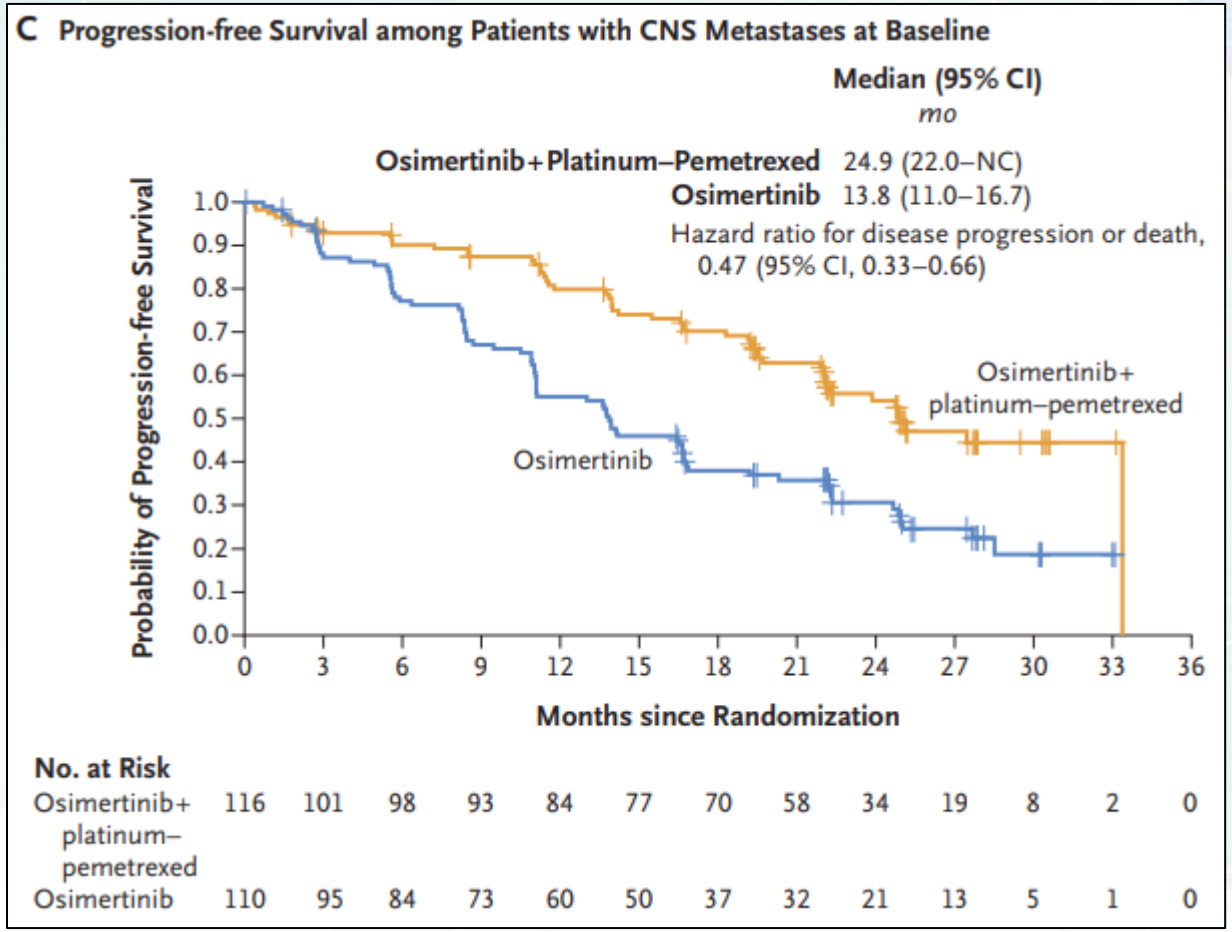
FLAURA2 Efficacy





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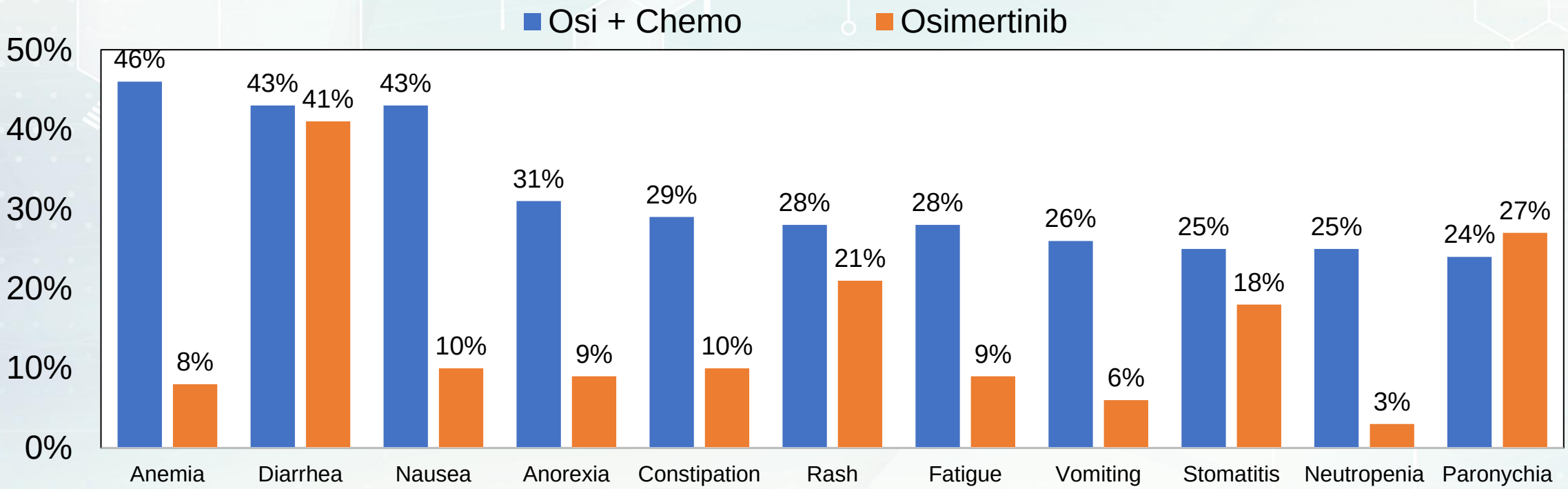
Planchard D,Y, et al. N Engl J Med. 2023;389(21):1935-1948.

FLAURA2 Safety



	Osi + Chemo*	Osimertinib
Osi dose interruptions	43%	19%
Osi dose reductions	10%	3%
Osi discontinuation	11%	6%

*median doses of chemotherapy: 4 cycles (platinum), 12 cycles (pemetrexed)

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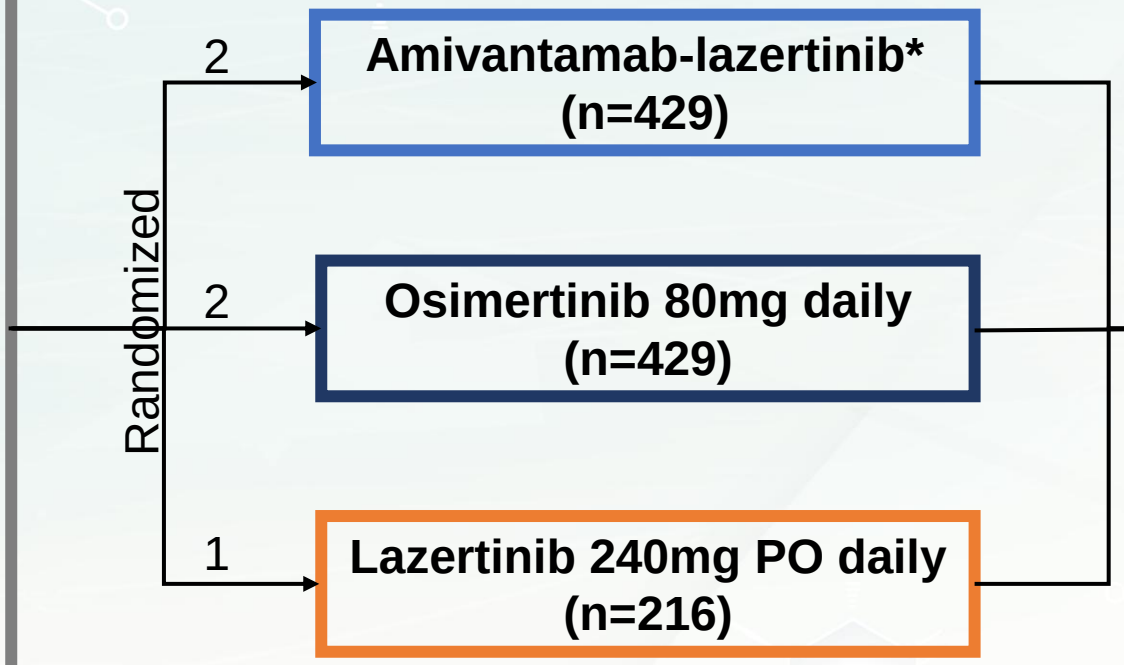
Planchard D,Y, et al. N Engl J Med. 2023;389(21):1935-1948.

MARIPOSA Design

Inclusion Criteria
- Locally advanced or metastatic NSCLC
- Treatment naïve
- EGFR exon19del or L858R
- ECOG PS 0-1

Stratified
- EGFR mutation type
- Asian race
- Brain metastasis



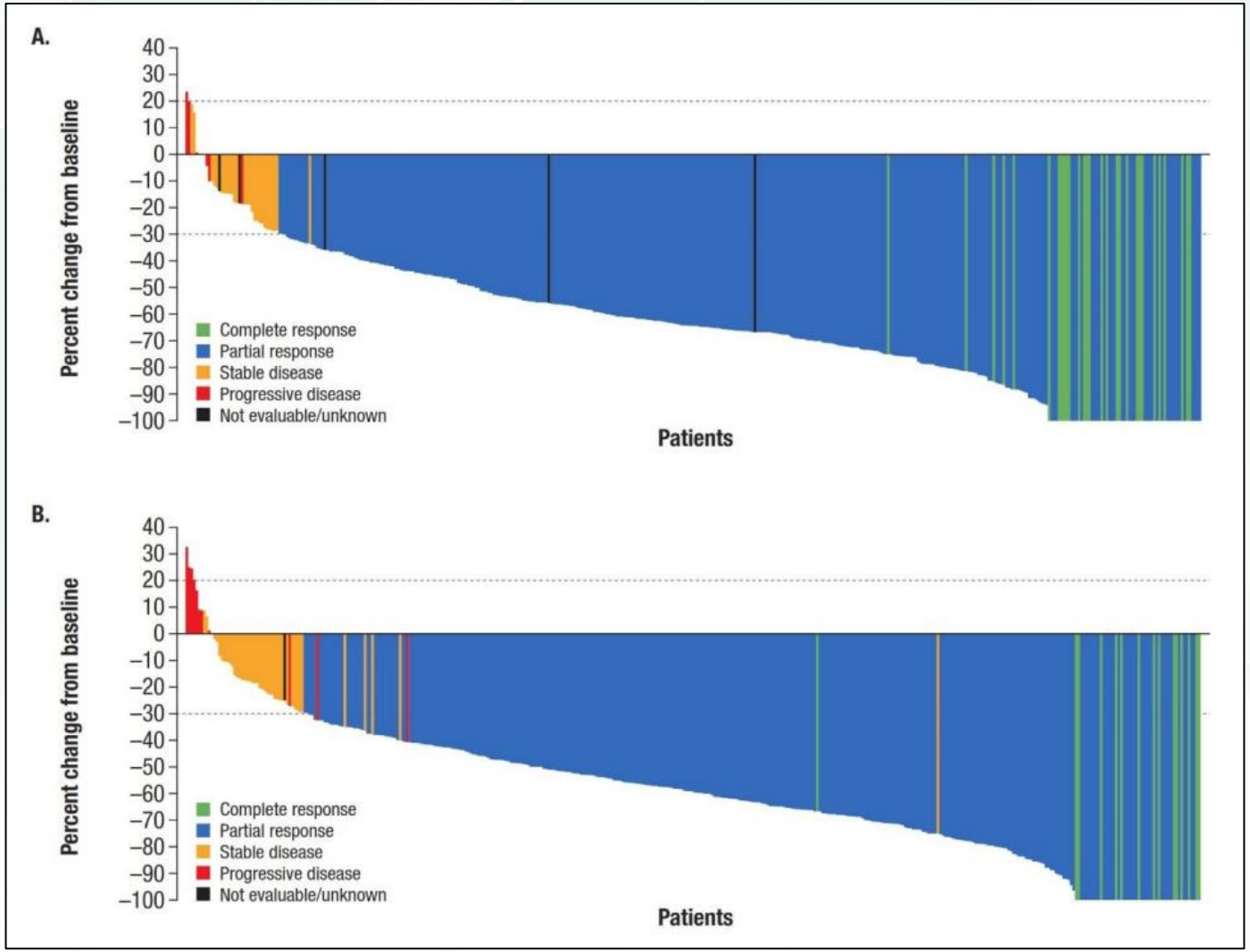
Primary Endpoint
- PFS by BICR

Secondary Endpoints
- Overall survival
- ORR
- Duration of response
- Intracranial PFS
- Safety

*Ami-Lazer Dosing (in 28d cycles)
Amivantamab: 1050/1400mg (≥80kg) IV weekly for C1 then q2wk
Lazertinib: 240mg PO daily

Cho BC, et al. N Engl J Med. 2024;391(16):1486-1498.

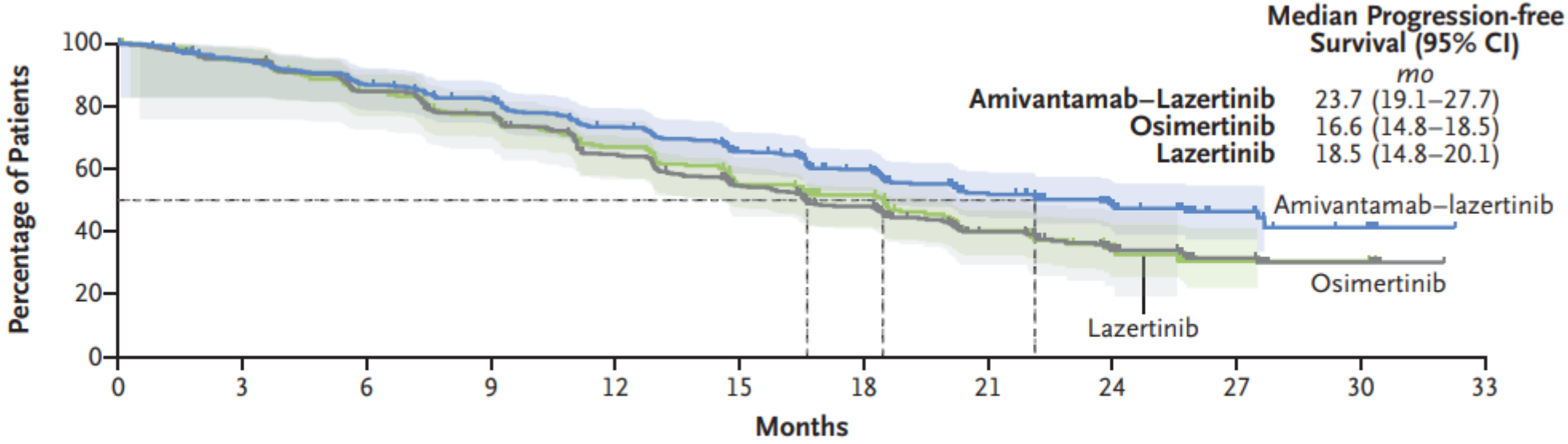
MARIPOSA Efficacy



Cho BC, et al. N Engl J Med. 2024;391(16):1486-1498.

MARIPOSA Efficacy

B **Progression-free Survival in Amivantamab–Lazertinib Group as Compared with the Osimertinib and the Lazertinib Monotherapy Groups**



No. at Risk											
Amivantamab–lazertinib	429	391	357	332	291	244	194	106	60	33	8	0
Osimertinib	429	404	358	325	266	205	160	90	48	28	10	0
Lazertinib	216	200	174	157	134	103	83	41	19	6	2	0

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Cho BC, et al. N Engl J Med. 2024;391(16):1486-1498.

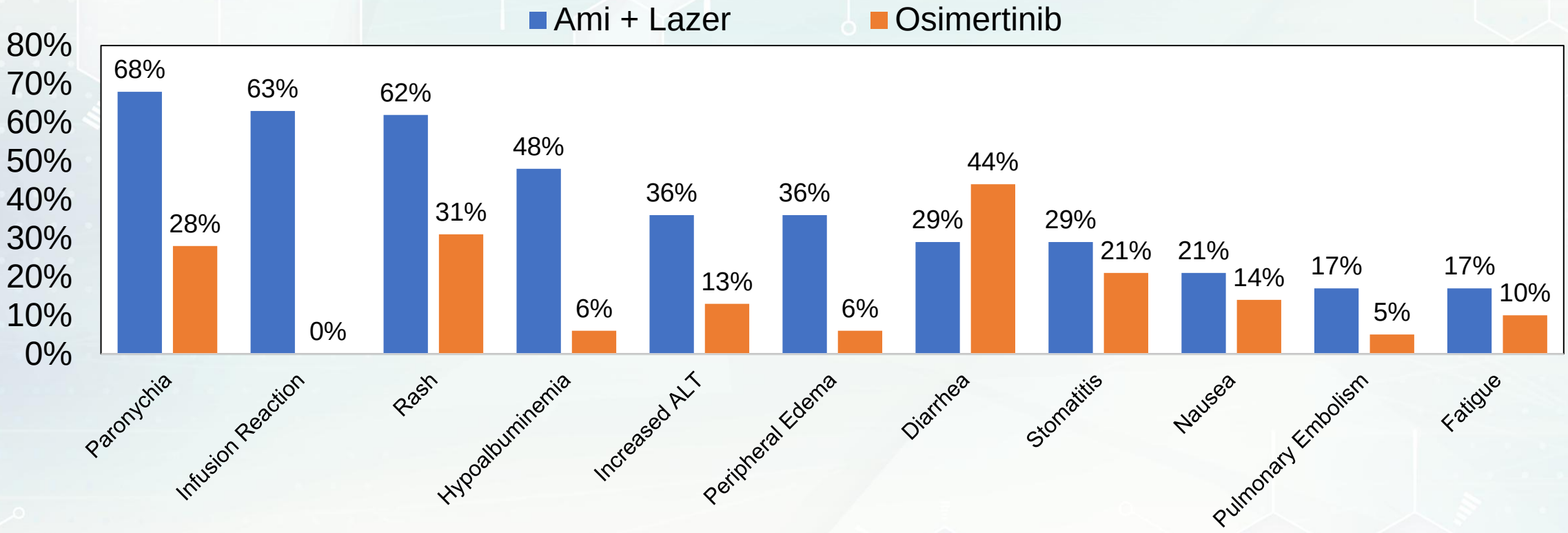
MARIPOSA High-Risk Groups

Patient Characteristics	Amivantamab + Lazertinib	Osimertinib
High risk features*	20.3 months	15.0 months
	0.72 (0.58–0.90)	
TP53 mutation	18.2 months	12.9 months
	0.65 (0.48–0.86)	
Brain Metastasis	18.3 months	13.0 months
	0.69 (0.53–0.92)	
Liver Metastasis	18.2 months	11.0 months
	0.58 (0.37–0.91)	
Baseline ctDNA detected	20.3 months	14.8 months
	0.68 (0.53–0.86)	

*high risk features identified in ~85% of patients in the MARIPOSA trial

Cho BC, et al. N Engl J Med. 2024;391(16):1486-1498; Felip E, et al. Ann Oncol. 2024;35(9):805-816.

MARIPOSA Safety



	Ami + Lazer	Chemotherapy
Dose Interruptions	83%	39%
Dose Reductions	59%	5%
Discontinuation	35%	14%

Cho BC, et al. N Engl J Med. 2024;391(16):1486-1498.

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Front-line Regimens

Osimertinib	Osimertinib + Chemotherapy	Amivantamab + Lazertinib
ORR: 80%	ORR: 83%	ORR: 86%
mPFS: 18.9mo	mPFS: 25.5mo	mPFS: 23.7mo
mOS: 38.6mo	mOS: NR	mOS: NR

Soria JC,, et al. N Engl J Med. 2018;378(2):113-125; Ramalingam SS, et al. N Engl J Med. 2020;382(1):41-50; Planchard D,Y, et al. N Engl J Med. 2023;389(21):1935-1948; Cho BC, et al. N Engl J Med. 2024;391(16):1486-1498.

Drug Toxicities

EGFR TKI

Rash

Diarrhea

Paronychia

Stomatitis

Chemotherapy

Nausea & vomiting

Myelosuppression

Fatigue

Taste/Appetite changes

Amivantamab

EGFR toxicities

Edema

Infusion reactions

VTE (with EGFR TKI)

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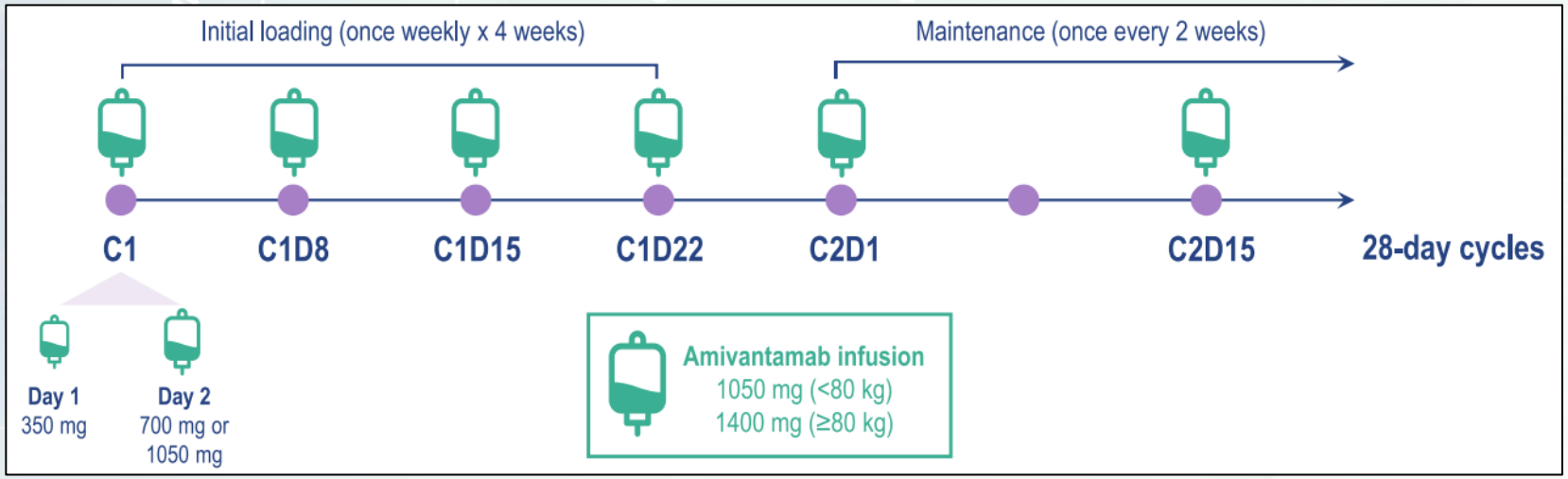
Soria JC,, et al. N Engl J Med. 2018;378(2):113-125; Ramalingam SS, et al. N Engl J Med. 2020;382(1):41-50; Planchard D,Y, et al. N Engl J Med. 2023;389(21):1935-1948; Cho BC, et al. N Engl J Med. 2024;391(16):1486-1498.

Time Toxicity

Amivantamab + Lazertinib



Estimated Infusion Chair Time

C1D1	C1D2	C1D8	C1D15	C1D22	C2+
~4-6h	~6-8h	~4-5h	~3-4h	~2.5h	~2.5h

Osimertinib + Chemotherapy

Anti-emetics: ~30-60min
Pemetrexed: 10min
Carboplatin: ~30-60min
OR
Cisplatin: ~30-60min
IV hydration (pre-post): ~2h

Total time: ~2-3h (Carboplatin) or ~4-5h (Cisplatin)

Park K, et al. Lung Cancer. 2023;178:166-171.

Preventing AEs with Amivantamab + Lazertinib

Begin Amivantamab + Lazertinib

IRR Prophylactic Regimen (SKIPPirr)[1]	VTE Prophylactic Regimen (PALOMA-2, PALOMA-3)[2,3]
2 Days to 1 hour before start Oral 8-mg dexamethasone BID 2 days and 1 day prior and 8-mg 1 hour before first infusion[a]	**First 4 months** Oral anticoagulants as per NCCN or local guidelines

Dermatologic Prophylactic Regimen (COCOON)[b]

Antibiotic prophylaxis	**Weeks 1–12** 100-mg BID doxycycline or minocycline	**Weeks 13+** 1% Topical clindamycin lotion on the scalp daily
Nail cleaning agent	**Weeks 1+** 4% Chlorhexidine on the fingernails and toenails daily for 12 months	
Long-acting skin hydration	**Weeks 1+** Ceramide-based moisturizer at least daily for 12 months[c]	

[a]Includes standard premedication (antihistamines, antipyretics, and glucocorticoids). [b]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID; topical clindamycin lotion 1% on scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization: La Roche Posay Lipikar AP+M moisturizer on the body and face at least daily. [c]La Roche Posay Lipikar AP+M moisturizer was used in COCOON.

BID, twice daily; IRR, infusion-related reaction; VTE, venous thromboembolism.

1. Spira AI, et al. *J Thorac Oncol*. 2025:S1556-0864(25)00051-6. 2. Scott SC, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA.
3. Leighl NB, et al. *J Clin Oncol*. 2024 Oct 20;42(30):3593-3605.

Risk-Adapted Approach

Osimertinib Monotherapy	Chemo+Osimertinib	Amivantamab + Lazertinib
EGFR ex19del		*EGFR* L858R
TP53 wide type		*TP53* mutant
Baseline ctDNA negative		Baseline MET amplification
No brain metastasis		Baseline ctDNA positive
Low disease burden		Brain metastasis
Poor performance status		Large tumor burden
Multiple comorbidities		Good performance status
		No comorbidities

Increasing Toxicity

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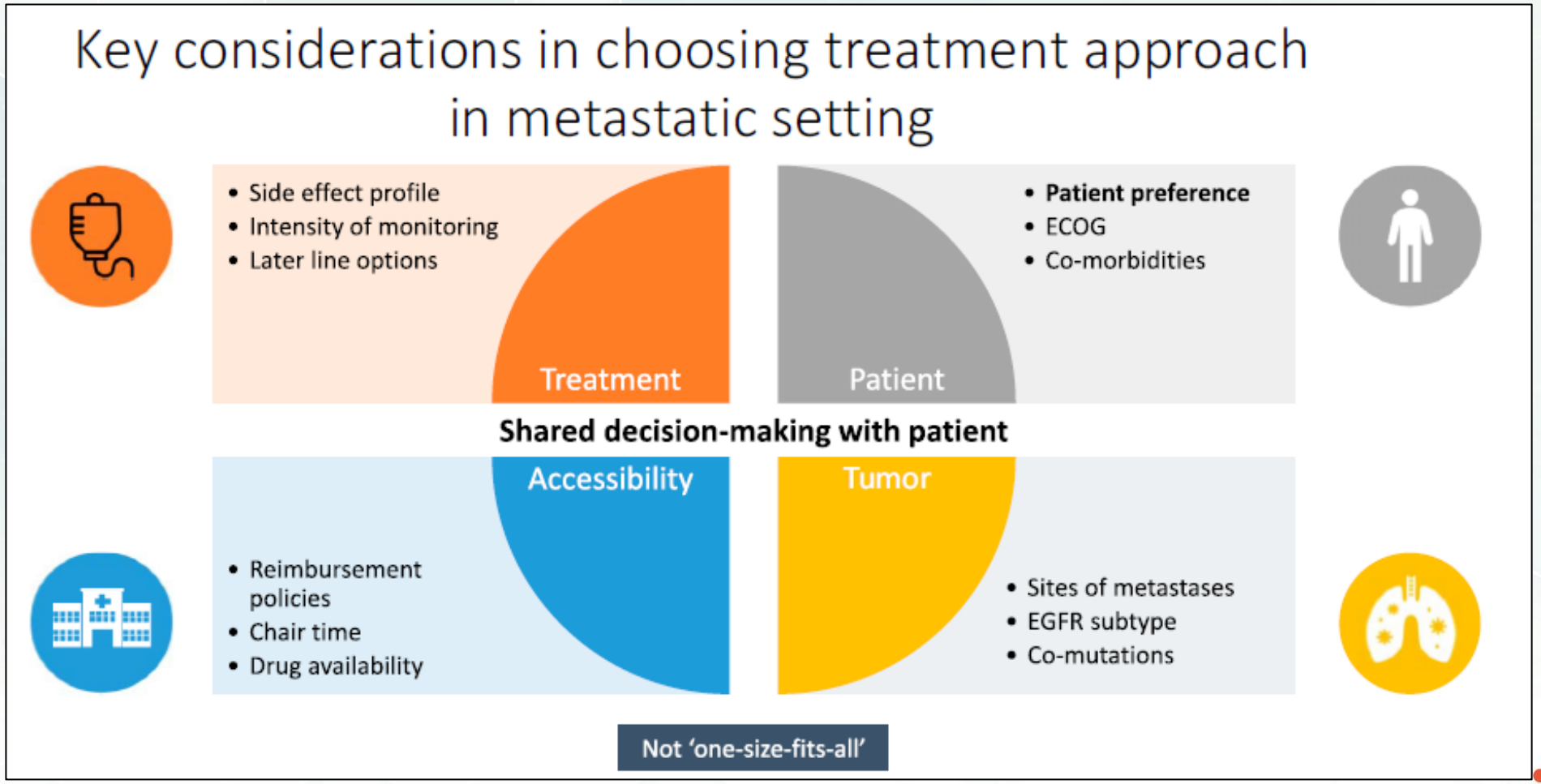
Chen MF, et al. Ann Oncol. 2024;35(1):4-6

Patient Case

- SH is a 49-year-old never-smoking female with newly-diagnosed NSCLC. PET/MRI show avid lesions in her right lower lobe, mediastinal lymph nodes, liver, left iliac crest, and right temporal lobe. Comprehensive molecular testing revealed an EGFR exon19 deletion and TP53 loss-of-function mutation. She presents to her medical oncologist to discuss first-line treatment options for her cancer.

- She has an excellent performance score (ECOG: 0), with no other medical comorbidities and wants to pursue aggressive treatment. She would like to prefer avoiding her friends and co-workers knowing she has lung cancer.

Shared Decision Making



Saw SPL, et al. Am Soc Clin Oncol Educ Book. 2024;44(3):e432516.

Subsequent Treatments

Patient Case

- SH is a 49-year-old never-smoking female with widely metastatic EGFR-mutant NSCLC. She was started on first-line carboplatin, pemetrexed, and osimertinib given the presence of brain metastasis and TP53 mutation at baseline.

- Restaging scans performed ~2 years after she started treatment demonstrated two new hypodense lesions in her liver concerning for disease progression.

QUESTION 2

What is the next best treatment option for patient SH after progressing on front-line osimertinib + chemotherapy?

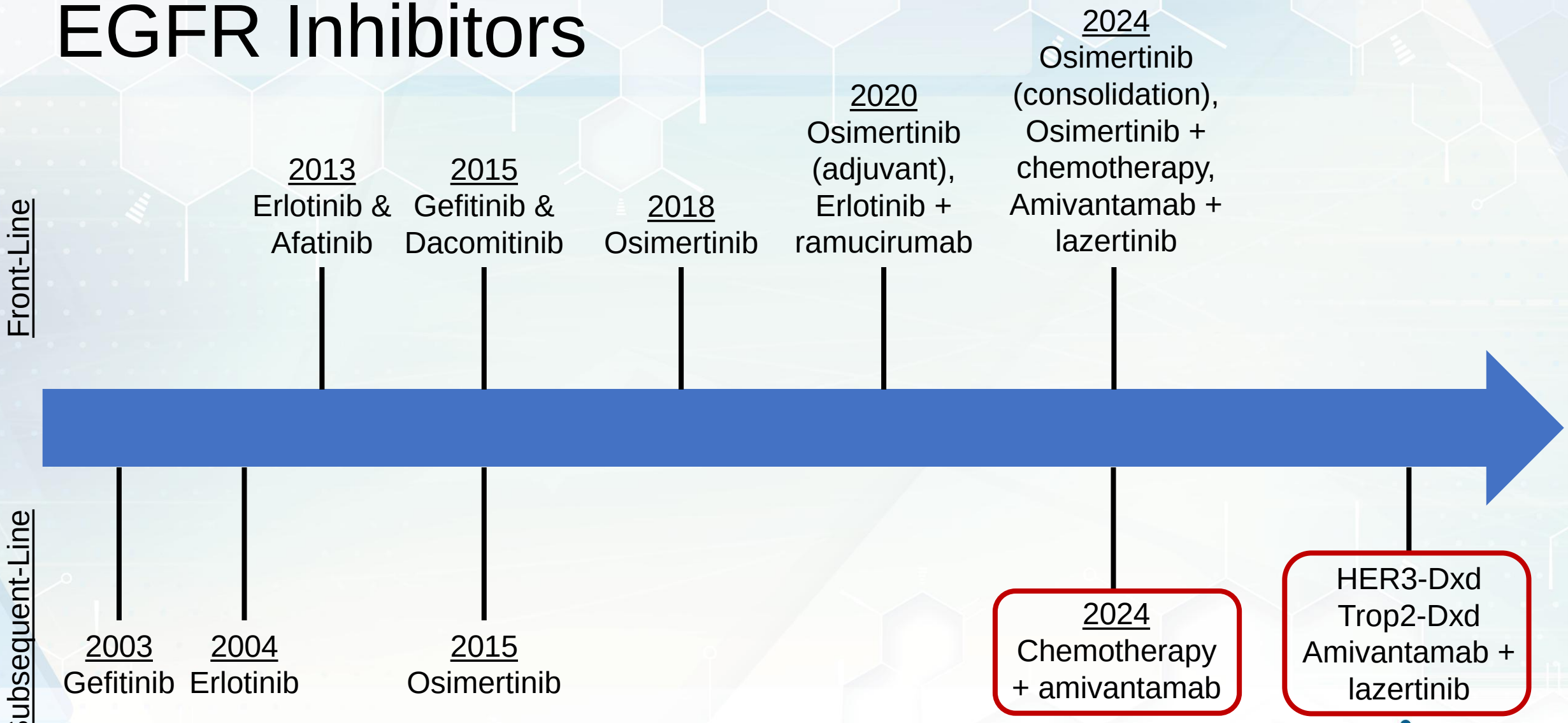
A) Local therapy and continue osimertinib

B) Chemotherapy + amivantamab

C) Amivantamab + lazertinib

D) HER3 or TROP2 directed antibody-drug conjugate

EGFR Inhibitors



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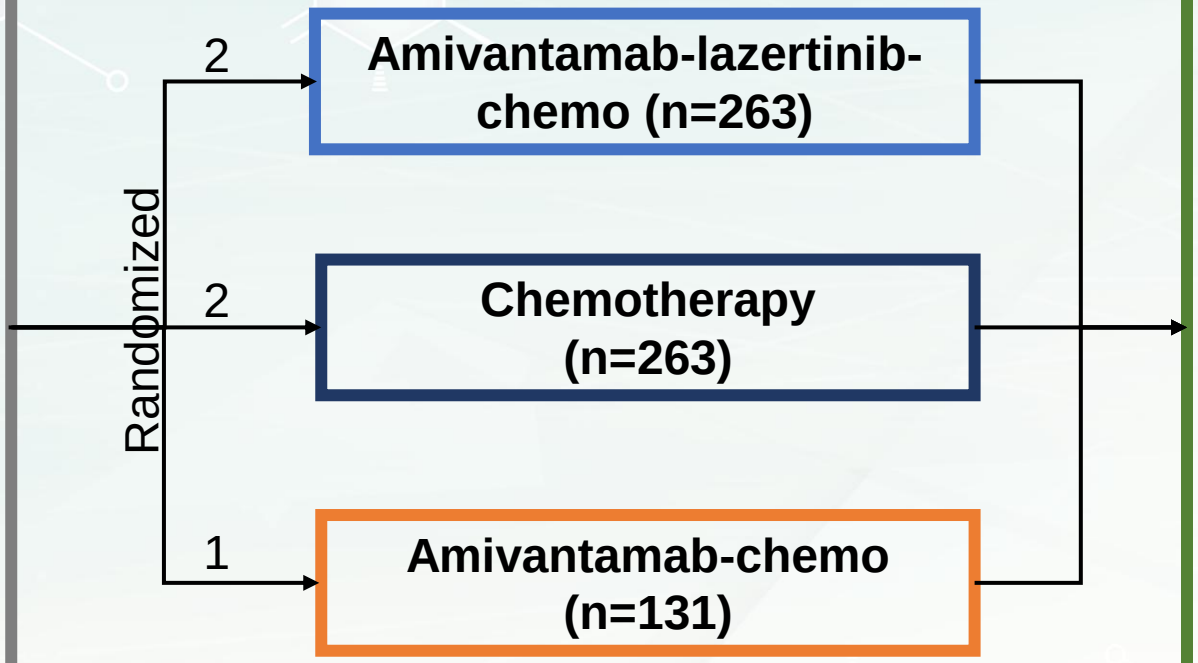
MARIPOSA-2 Design

Inclusion Criteria

- Locally advanced or metastatic NSCLC
- Immediately progressed on osimertinib
- EGFR exon19del or L858R
- ECOG PS 0-1

Stratified

- 1L vs 2L osimertinib
- Asian race
- Brain metastasis



Primary Endpoint

- PFS by BICR (ami-lazer-chemo vs chemo)
- PFS by BICR (ami-chemo vs chemo)

Secondary Endpoints

- Overall survival
- ORR
- Duration of response
- Intracranial PFS
- Safety

Treatment Dosing (in 21d cycles)

Amivantamab: 1400/1750mg (≥80kg) IV weekly for C1&2, then 1750mq/2100mg (≥80kg) q3wk for C3+

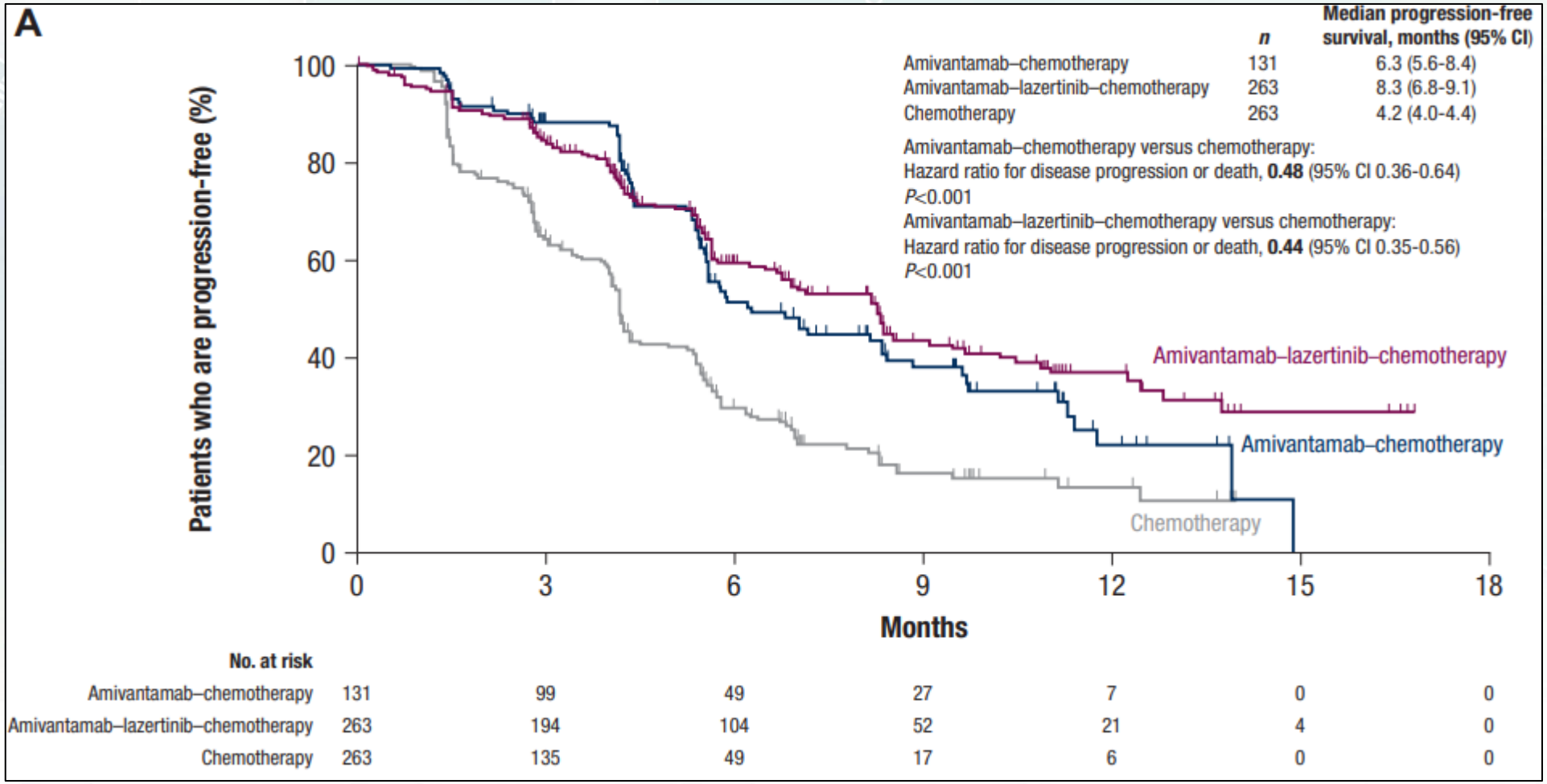
Lazertinib: 240mg PO daily starting C5+

Chemotherapy:

- **Carboplatin** AUC5 IV D1 for 4 cycles
- **Pemetrexed** 500mg/m2 IV D1 until disease progression

Passaro A, et al. Ann Oncol. 2024;35(1):77-90.

MARIPOSA-2 Efficacy



Passaro A, et al. Ann Oncol. 2024;35(1):77-90.

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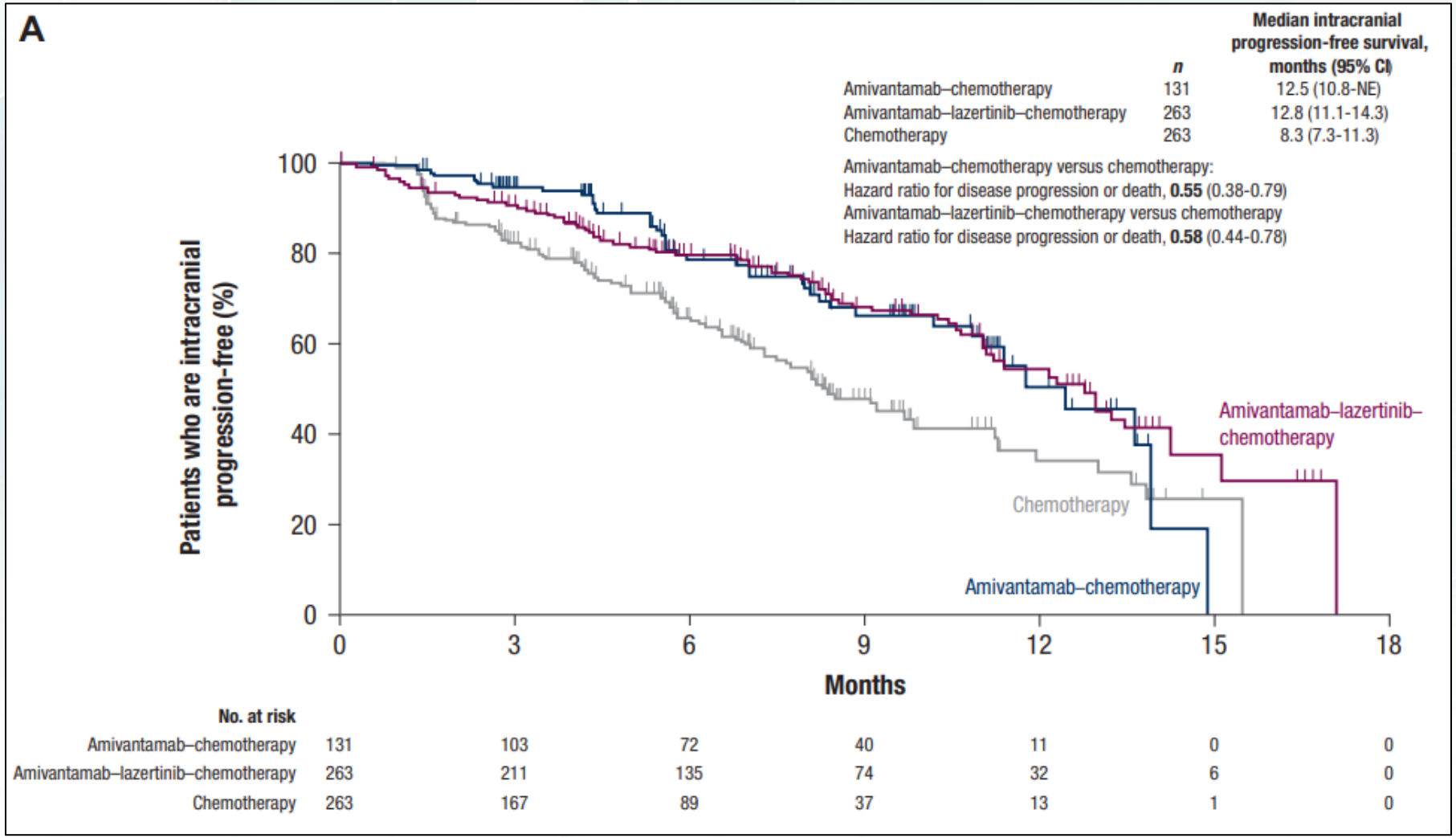
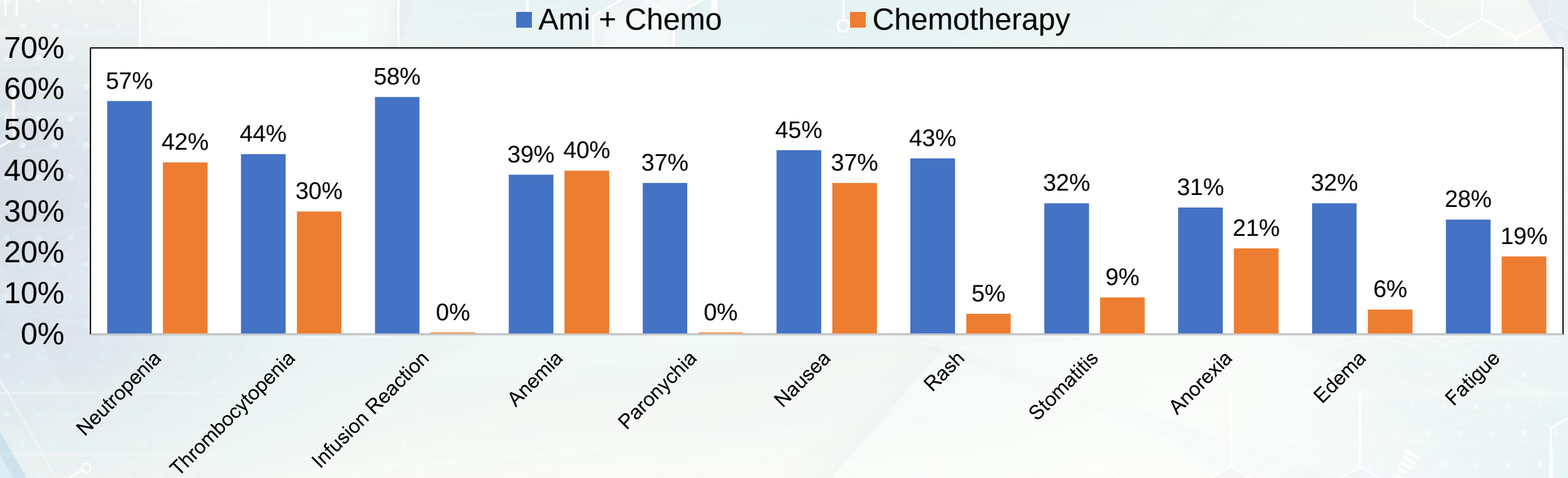
MARIPOSA-2 Efficacy



Passaro A, et al. Ann Oncol. 2024;35(1):77-90.

MARIPOSA-2 Safety



	Ami + Chemo	Chemotherapy
Dose Interruptions	63%	33%
Dose Reductions	41%	15%
Discontinuation	18%	4%

Passaro A, et al. Ann Oncol. 2024;35(1):77-90.

Antibody Drug Conjugate Efficacy

HERTHENA-Lung01

- Advanced/metastatic NSCLC, EGFR exon19del/L858R, ≥1 prior EGFR TKI & platinum-based chemotherapy
- Patritumab deruxtecan (HER3-Dxd): 5.6 mg/kg IV q3wks
- ORR: 29.8%, CNS ORR: 33%, mPFS: 5.5mo, mOS: 11.9mo

TROPION-Lung05

(EGFR subset)

- Advanced/metastatic NSCLC, EGFR mutation, 1-2 prior EGFR TKIs & cytotoxic therapies (including platinum doublet)
- Datopotamab deruxtecan (TROP2-Dxd): 6.0 mg/kg IV q3wks
- ORR: 43.6%, mPFS: 5.8mo, mOS: 18.3mo

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Yu HA, et al. J Clin Oncol. 2023;41(35):5363-5375; Sands J, et al. J Clin Oncol. 2025:JCO2401349.

Antibody Drug Conjugate Toxicities

HER3-Dxd

Adverse Event (all grade)	Patritumab Deruxtecan (n=225)
Nausea	66%
Thrombocytopenia	44%
Anorexia	42%
Neutropenia	36%
Constipation	34%
Anemia	33%
Fatigue	31%
Diarrhea	28%
Alopecia	25%
Stomatitis	12%
ILD	5.3%

TROP2-Dxd

Adverse Event (all grade)	Datopotamab Deruxtecan (n=137)
Stomatitis	65.7%
Nausea	54.7%
Alopecia	49.6%
Ocular events	26.3%
Anorexia	20.4%
Fatigue	19.0%
Infusion reaction	16.1%
Constipation	15.3%
Rash	13.9%
ILD	3.6%

Yu HA, et al. J Clin Oncol. 2023;41(35):5363-5375; Sands J, et al. J Clin Oncol. 2025:JCO2401349.

PALOMA-3

Trial design: phase 3, international, randomized trial assessing the noninferiority of pharmacokinetics, efficacy, and safety

Inclusion: ≥18 years old, locally advanced or metastatic NSCLC, *EGFR* ex19del or L858R, asymptomatic or stable brain metastases, progression on osimertinib

Amivantamab SQ + Lazertinib 240mg daily (n = 206)

Amivantamab IV + Lazertinib 240mg daily (n = 212)

Continue treatment until disease progression or unacceptable toxicity

Outcome	Amivantamab SQ + Lazertinib	Amivantamab IV + Lazertinib
ORR	30%	33%
mPFS	6.1 months	4.3 months
	0.84 (0.64–1.10); P = 0.20	
OS at 12 months	65%	51%
	0.62 (0.42–0.92); P = 0.02	
IRR	13%	66%
Median duration of administration	4.8 minutes	5.0 hours (C1D1) 2.3 hours (C3D1)

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Leighl NB, et al. Clin Oncol. 2024 Oct 20;42(30):3593-3605

Other Chemotherapy Combinations

- Platinum-based doublet chemotherapy is standard of care for lung cancer treatment
  - Addition of bevacizumab provides modest PFS & OS benefit
- Chemo-immunotherapy is ineffective for EGFR-mutant NSCLC
  - Keynote789: second-line chemo + pembrolizumab post-EGFR TKI → **no PFS or OS benefit**
  - Checkmate722: second-line chemo + nivolumab post-EGFR TKI → **no PFS or OS benefit**
- Unclear role of chemotherapy in combination with immunotherapy & VEGF inhibition
  - IMPower150: first-line carbo/taxol/bev/atezo → **PFS benefit in EGFR/ALK+ patients, but no OS benefit**
  - IMPower151: first-line carbo/taxol/bev/atezo → **no PFS benefit seen in EGFR/ALK+ patients**
  - ATTLAS: second-line carbo/pem/bev/atezo post-EGFR/ALK TKI → **PFS benefit but no OS benefit**
  - ORIENT-31: second-line carbo/pem/bev(biosim)/sintilimab post-EGFR/ALK TKI → **PFS benefit but no OS benefit**
  - HARMONi-A: second-line carbo/pem/ivonescimab (PD-1/VEGF) post-EGFR/ALK TKI → **PFS benefit but OS data is immature**

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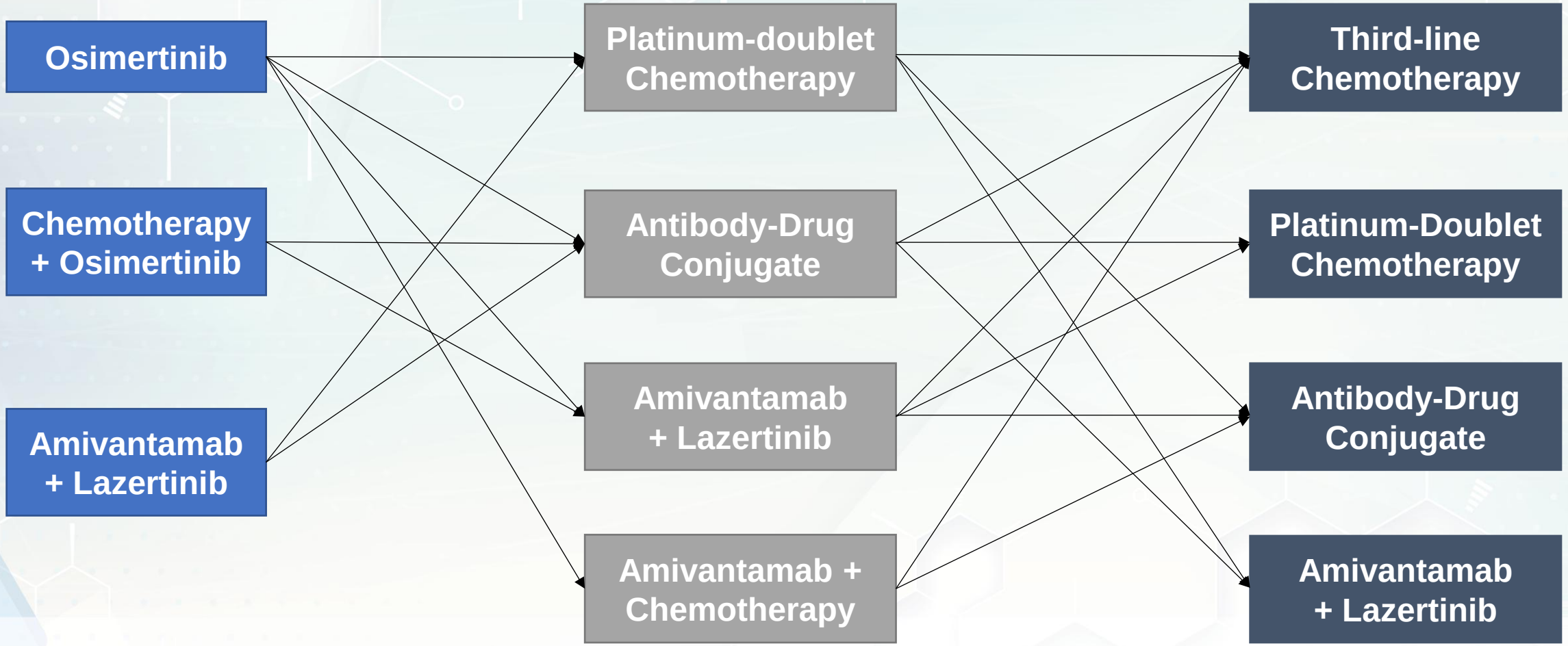
Socinski MA, et al. N Engl J Med. 2018;378(24):2288-2301; Nogami N, et al. J Thorac Oncol. 2022;17(2):309-323; Mok T, et al. J Clin Oncol. 2024;42(11):1252-1264; Park S, et al. J Clin Oncol. 2024;42(11):1241-1251; Lu S, et al. Lancet Respir Med. 2023;11(7):624-636; Yang JCH, et al. J Clin Oncol. 2023;41(17):suppl.LBA9000; Zhou C, et al. J Thorac Oncol. 2022;18(11):S64-S65.; Fang W et al. JAMA. 2024;332(7):561-570.

Treatment Sequencing



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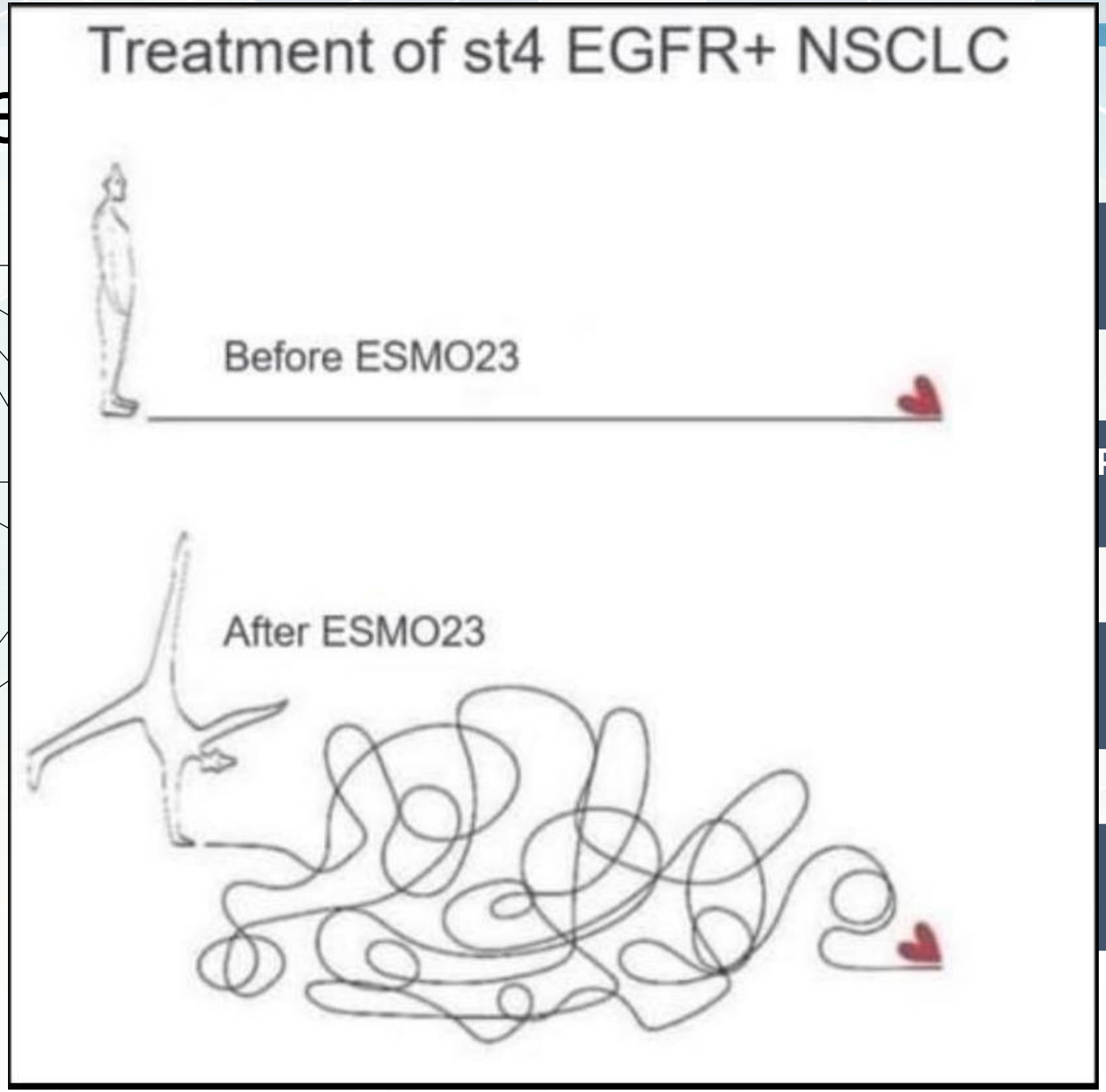
Chen MF, et al. Ann Oncol. 2024;35(1):4-6

Treatme

Osimertinib

Chemotherapy + Osimertinib

Amivantamab + Lazertinib



Third-line Chemotherapy

Platinum-Doublet Chemotherapy

Antibody-Drug Conjugate

Amivantamab + Lazertinib

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Chen MF, et al. Ann Oncol. 2024;35(1):4-6

QUESTION 3

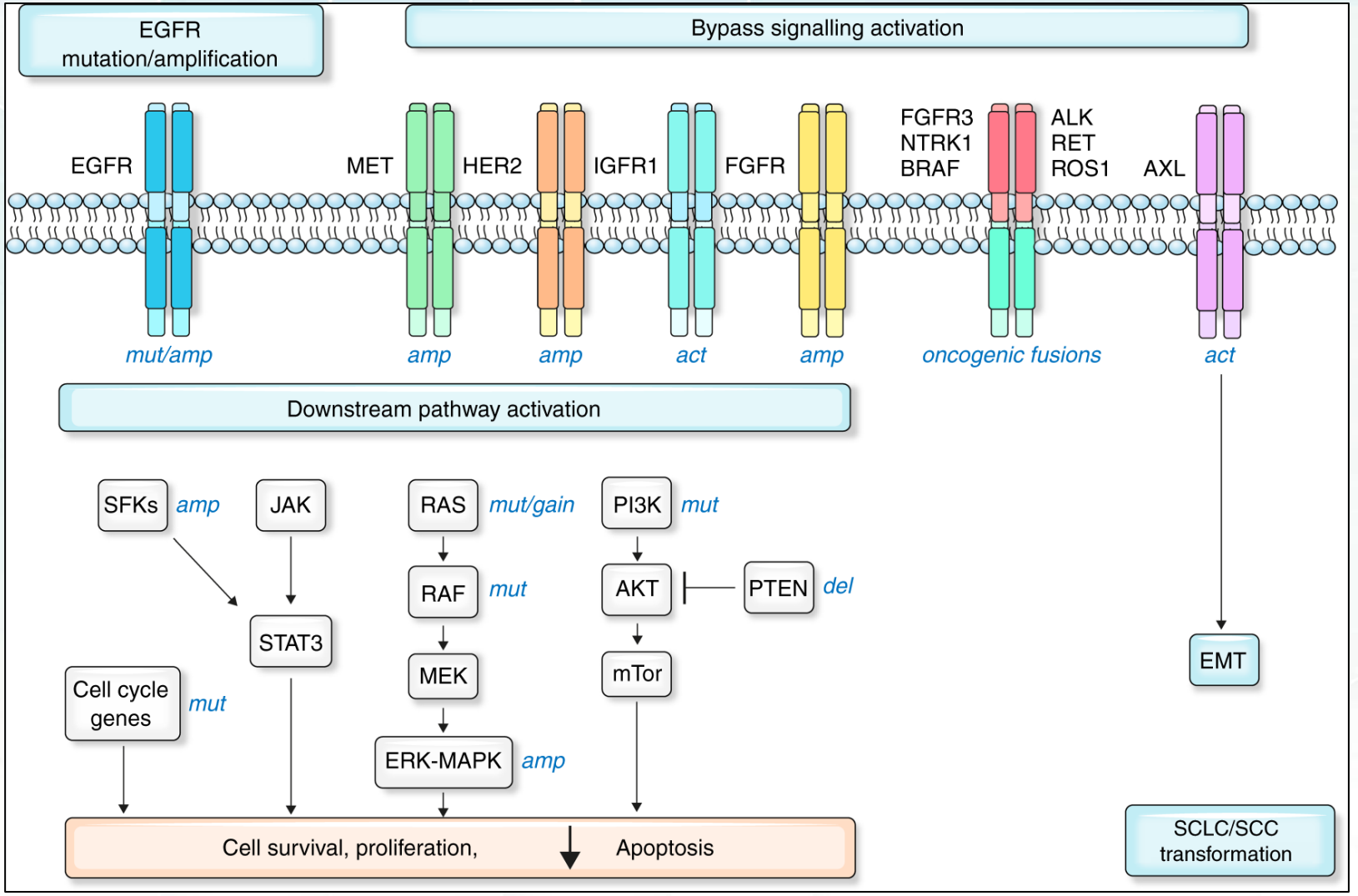
Do you repeat molecular sequencing after patients progress on front-line osimertinib treatment

A) Yes

B) No

C) Depends

Mechanisms of EGFR Resistance



Leonetti A, et al. Br J Cancer. 2019;121(9):725-737.

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Patient with advanced NSCLC with common EGFR mutation: *exon 19 deletion* or *exon 21 L858R*

1L

OSIMERTINIB (14)

OSIMERTINIB + CARBOPLATINE + PEMETREXED (37)

AMIVANTAMAB + LAZERTINIB (46)

New tumor sample or ctDNA at time of progression

(regardless of the first line)

Histological transformation

SCLC or SCC

2L

CARBO-ETOPOSIDE +/- OSI or +/- aPDL1

CARBO-PACLITAXEL +/- OSI or +/- aPDL1

Acquired resistance identified

C797S

Bypass

Mutation: *KRAS (G12C), BRAF(V600E)*

Fusion: *RET, ALK, ROS1*

MET amp.

No resistance mechanism identified

Acquired resistance identified

C797S

Bypass

Mutation: *KRAS (G12C), BRAF(V600E)*

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No resistance mechanism identified

Acquired resistance identified

C797S

Bypass

Mutation: *KRAS (G12C), BRAF(V600E)*

Fusion: *RET, ALK, ROS1*

MET amp.

No resistance mechanism identified

Consider inclusion in a clinical trial

Option 1

CARBOPLATINE + PEMETREXED + AMIVANTAMAB (20)

Other option (if MET+ IHC)

AMIVANTAMAB + LAZERTINIB (77)

Other option (according to acquired resistance mechanisms)

1st/4th gen EGFR TKI | TKI combination ? | **OSI + iMET** (71)

Other option

PATRITUMAB-DERUXTECAN (depending on Herthena-02 results)

Other option

CARBOPLATINE PEMETREXED +/- BEVACIZUMAB
Carboplatin-weekly paclitaxel for elderly patients

Option 1 (CHRYSALIS-2 cohort A)

AMIVANTAMAB + LAZERTINIB

Other option (according to acquired resistance mechanisms)

1st/4th gen EGFR TKI | TKI combination ? | **OSI + iMET** (71)

Other option

Chemotherapy

Other option (depending on clinical trials results)

PATRITUMAB-DERUXTECAN
DATOPOTAMAB-DERUXTECAN

Option 1

CARBOPLATINE PEMETREXED +/- BEVACIZUMAB
Carboplatin-weekly paclitaxel for elderly patients

Other option (according to acquired resistance mechanisms)

1st/4th gen EGFR TKI | TKI combination ? | **OSI + iMET** (71)

Other option (depending on clinical trials results)

PATRITUMAB-DERUXTECAN
DATOPOTAMAB-DERUXTECAN

3L

New tumor sample or ctDNA at time of progression

DATOPOTAMAB-DERUXTECAN (79)
PATRITUMAB-DERUXTECAN (82)

Second-line chemotherapy

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Wespiser M, et al. Lung Cancer. 2024;194:107895.

Treatment Considerations

- Prior Treatments
- Prior Responses
- Prior Tolerability
- Patient Preference
- Resistance Mechanism

Molecular Sequencing

Testing Considerations

- Who
  - Histology (non-squamous vs squamous)
- How
  - Tissue vs blood (ctDNA)
  - Single-gene vs broad panel
  - DNA vs RNA
- When
  - Non-metastatic
  - Metastatic disease
  - Disease recurrence

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Sample Considerations

Tissue	Blood (ctDNA)*
Advantages: - Tumor specific - Improved sensitivity Disadvantages: - Longer turnaround time - Invasive biopsy required - Cannot use certain samples (e.g. bone) - Cannot assess tumor heterogeneity	Advantages: - Non-invasive - Shorter turnaround time - Reflects tumor heterogeneity Disadvantages: - Sensitivity varies based on tumor burden - May contain false positives (e.g. CHIP) - Difficulty detecting fusions or amplifications

*unable to determine histologic transformation using ctDNA assay

Hofman P, Cancers (Basel). 2024;16(19):3340.

Patient Case

- JR is a 65-year-old male with newly diagnosed NSCLC. Comprehensive molecular sequencing and PD-L1 22C3 IHC revealed the following:
  - PD-L1: 90%
  - TMB: 15 mut/Mb
  - EGFR: A763_Y764insFQEA
  - TP53: P151S

- Are you comfortable selecting a first-line treatment option for this patient?

Patient Case

- JR is a 65-year-old male with newly diagnosed NSCLC. Comprehensive molecular sequencing and PD-L1 22C3 IHC revealed the following:
  - PD-L1: 90%
  - TMB: 15 mut/Mb
  - EGFR: A763_Y764insFQEA (exon 20 insertion)
  - TP53: P151S

- Are you comfortable selecting a first-line treatment option for this patient?

Sequencing Results

Lung Sample Patient 22024

Diagnosis: **Adenocarcinoma**

Accession No.: **Lung 22024**

xT

Date of Birth
11/22/1961

Sex
Male

Physician
Dr. Patel

Institution
Chicago Cancer Center

TEMPUS | xT
648 gene panel

Tumor specimen:
Lung, right upper lobe

Collected 3/3/2022
Received 3/16/2022
Tumor Percentage: 40%

Normal specimen:
Blood
Collected 3/9/2022
Received 3/11/2022

GENOMIC VARIANTS

Somatic - Potentially Actionable		Variant Allele Fraction
KRAS	p.G12C Missense variant (exon 2) - GOF	23.8%

Somatic - Biologically Relevant		
ARID2	p.W266* Stop gain - LOF	26.7%
RBM10	p.E808* Stop gain - LOF	25.5%
STK11	p.R331fs Frameshift - LOF	15.7%
NFE2L2	p.G81V Missense variant - GOF	12.6%
FAT1	c.13139-1G>T Splice region variant - LOF	10.7%
BCL11B	p.T502fs Frameshift - LOF	8.0%

Germline - Pathogenic / Likely Pathogenic

No germline pathogenic variants were found in the limited set of genes on which we report.

Pertinent Negatives

No pathogenic single nucleotide variants, indels, or copy number changes found in:

EGFR · BRAF · ALK · ROS1 · RET · MET · ERBB2 (HER2)

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden: 7.4 m/MB — 76th percentile

Microsatellite Instability Status: Stable | Equivocal | High

PATIENT

TUMOR TYPE: Lung non-small cell lung carcinoma (NOS)

REPORT DATE

ORDERED TEST #

PATIENT
DISEASE Lung non-small cell lung carcinoma (NOS)
NAME
DATE OF BIRTH
SEX
MEDICAL RECORD #

PHYSICIAN
ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT
MEDICAL FACILITY ID
PATHOLOGIST

SPECIMEN
SPECIMEN ID
SPECIMEN TYPE
DATE OF COLLECTION
SPECIMEN RECEIVED

PATIENT RESULTS

- 12 genomic findings
- 7 therapies associated with potential clinical benefit
- 0 therapies associated with lack of response
- 24 clinical trials

TUMOR TYPE: LUNG ADENOCARCINOMA

Genomic Alterations Identified†

EGFR C797S, exon 19 deletion (L747_T751del)
PIK3CA E542K
AURKA amplification
MYC amplification – equivocal‡
ARFRP1 amplification
ARID1A R1950Q
GNAS amplification
TP53 R282P
ZNF217 amplification

Additional Findings†

Microsatellite status MS-Stable
Tumor Mutation Burden TMB-Low; 5 Muts/Mb

Additional Disease-relevant Genes with No Reportable Alterations Identified†

KRAS
ALK
BRAF
MET
RET
ERBB2
ROS1

† For a complete list of the genes assayed and performance specifications, please refer to the Appendix
‡ See Appendix for details

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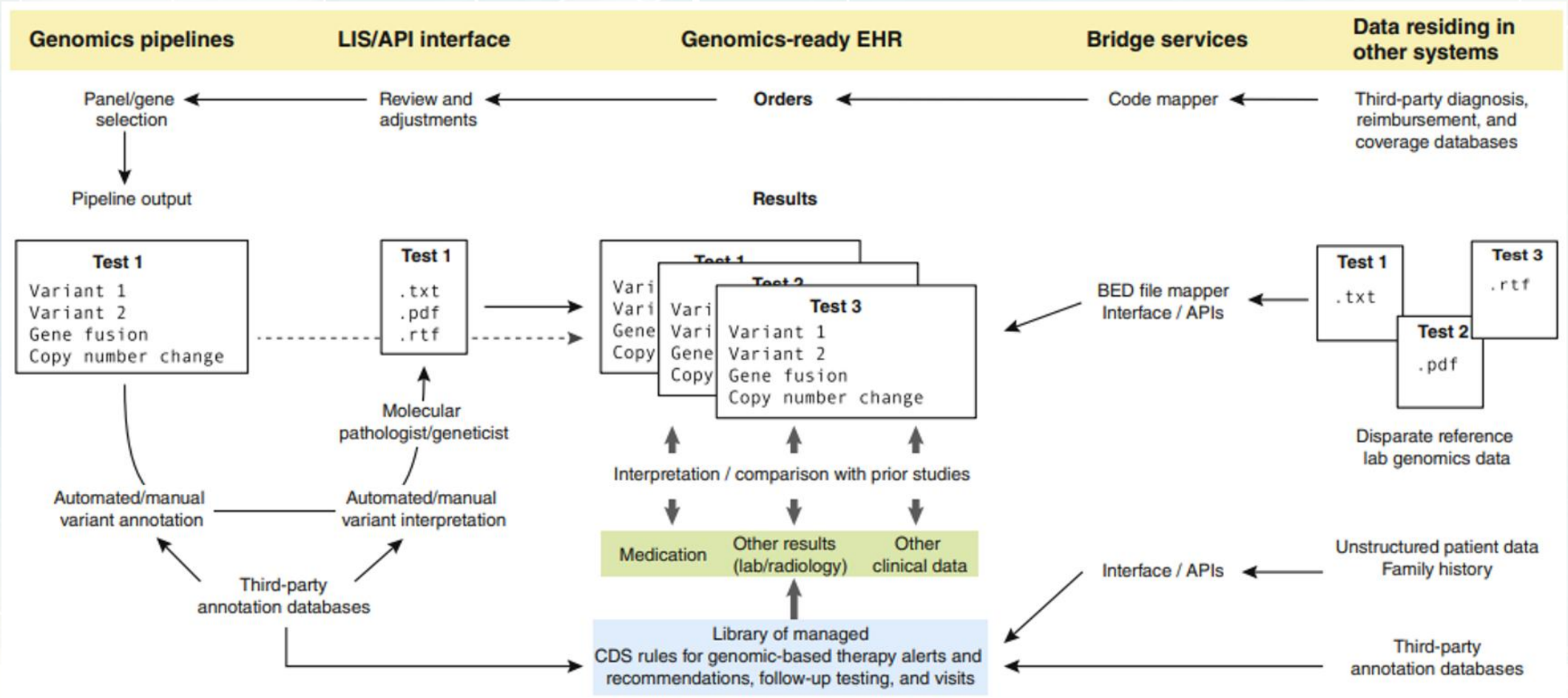
EMR Integration



Carter AB, J Mol Diagn. 2022;24(1):1-17.

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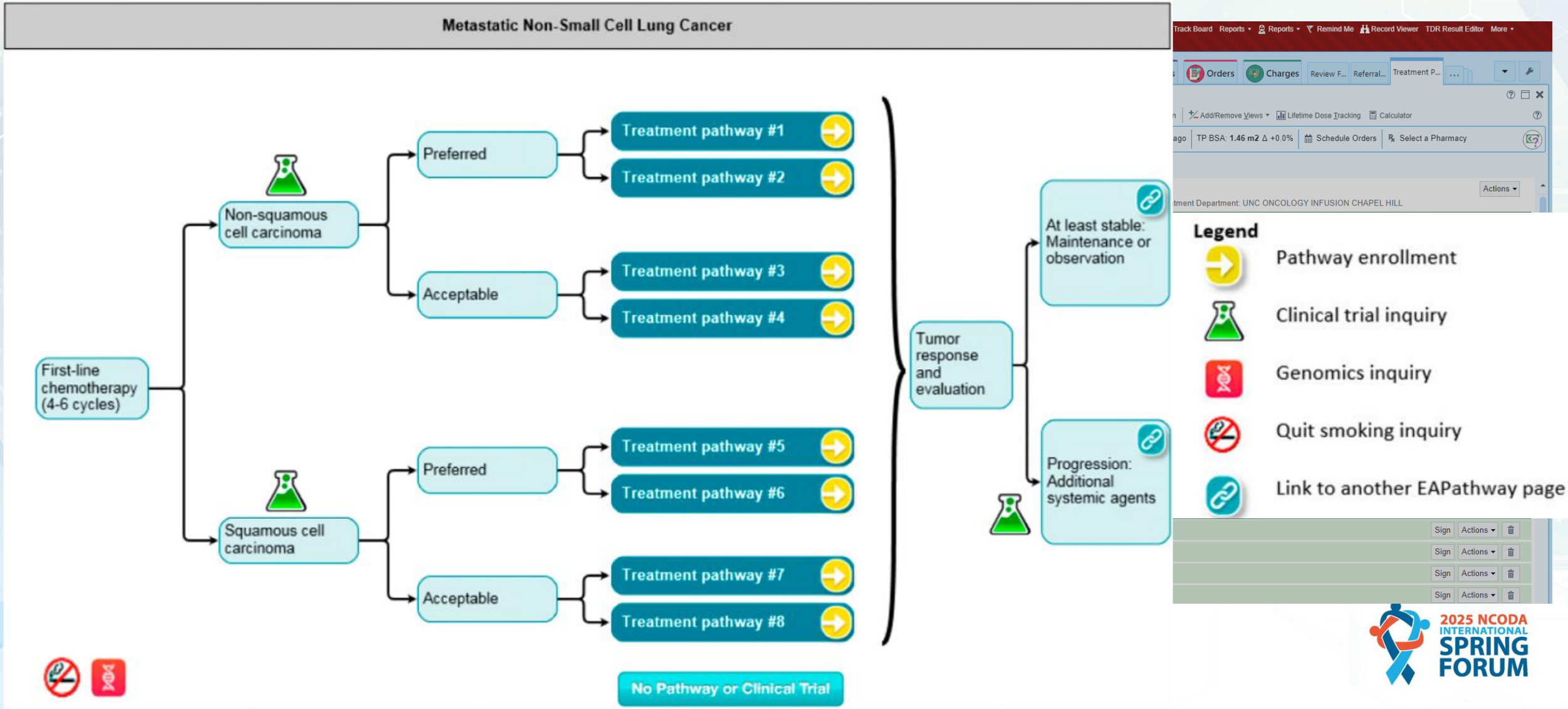
Clinical Decision Support



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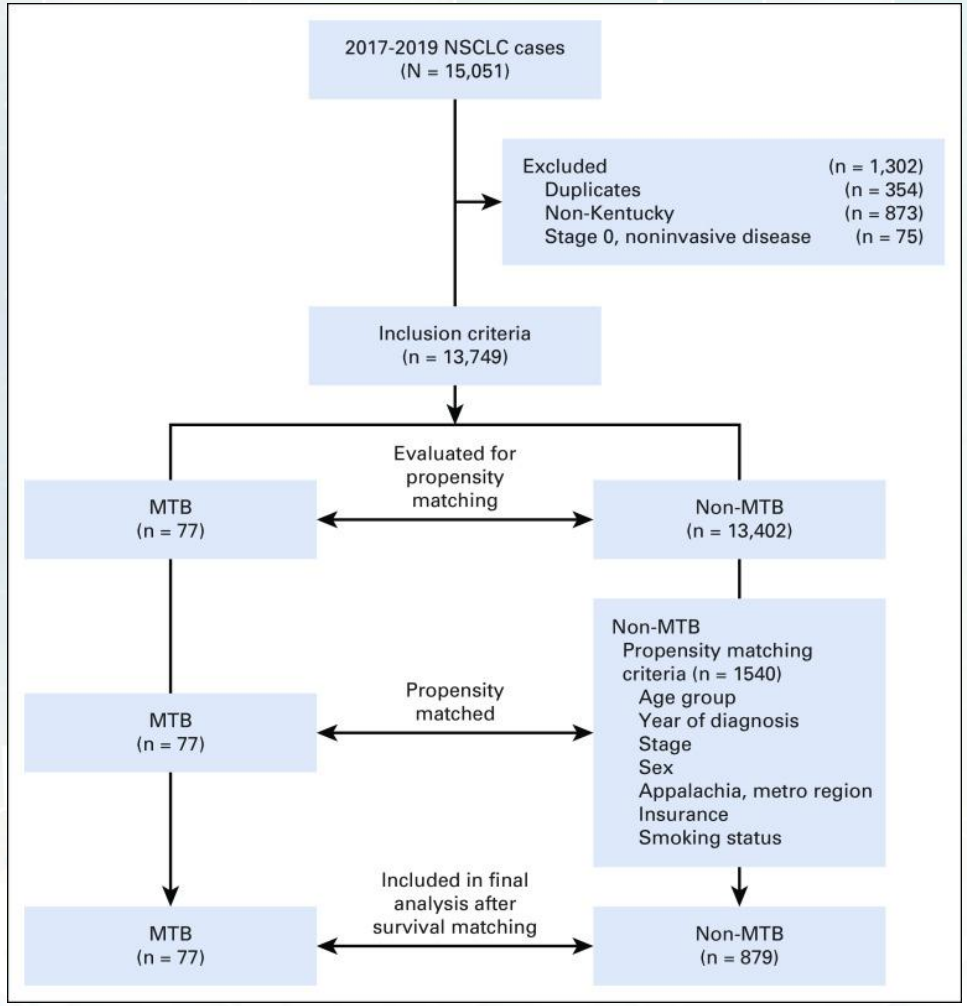
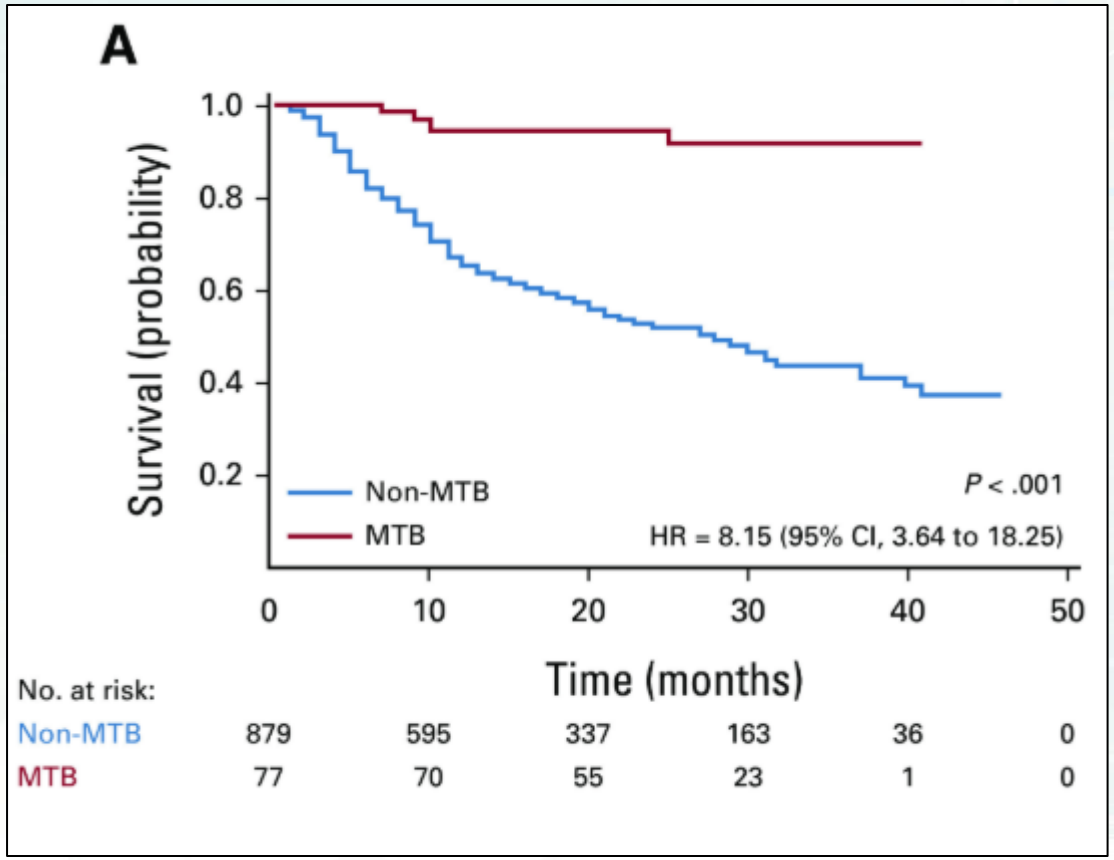
Molecular Tumor Boards





Huang B, JCO Precis Oncol. 2021;5:PO.21.00210

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SUMMARY

- Front-line intensification strategies have improved efficacy over osimertinib monotherapy
- Challenges in additional toxicities and complex administration warrant patient centered discussion to select optimal treatment
- Subsequent line therapies should consider prior therapies received and a patient's individual treatment goals
- Integrating molecular sequencing results into existing EMR platforms is challenging, but is essential for selection the optimal treatment
- Clinical decision support tools and molecular tumor boards may assist in selecting the most appropriate biomarker-directed therapies

QUESTION & ANSWER

Optimizing Patient Outcomes in EGFR and NSCLC Sequencing

Kevin Chen, PharmD, MS, BCOP, CPP

Clinical Pharmacist Practitioner

University of North Carolina
Medical Center

CE CODES

Optimizing Patient Outcomes in EGFR and NSCLC Sequencing