More Options, More Hope:
Understanding EGFR Treatments Today

EGFResisters

Recording Notice

Please be advised that this session of the *EGFR Resisters' Patient & Caregiver Summit* is being livestreamed and recorded.

Recordings will be made available on the EGFR Resisters website and accessible to the public.

By participating in this event, you consent to the recording and distribution of these sessions.

If you have any concerns, please speak with event staff.

EGFR esisters

Session Speaker

Christine Lovly, MD, PhD, FASCO
Moderator
Chief, Division of Thoracic Medical Oncology
City of Hope Comprehensive Cancer Center
Duarte, CA

EGFResisters

Session Objectives

1. Help patients and caregivers understand the treatments available today for *EGFR*-positive lung cancer.

2. Explain recent research advances in *EGFR*-positive lung cancer and what it means for patients and families across different stages and *EGFR* mutations.

EGFResisters

Please Send in Your Questions!

This QR code will be live throughout the session

Download the Slides Here

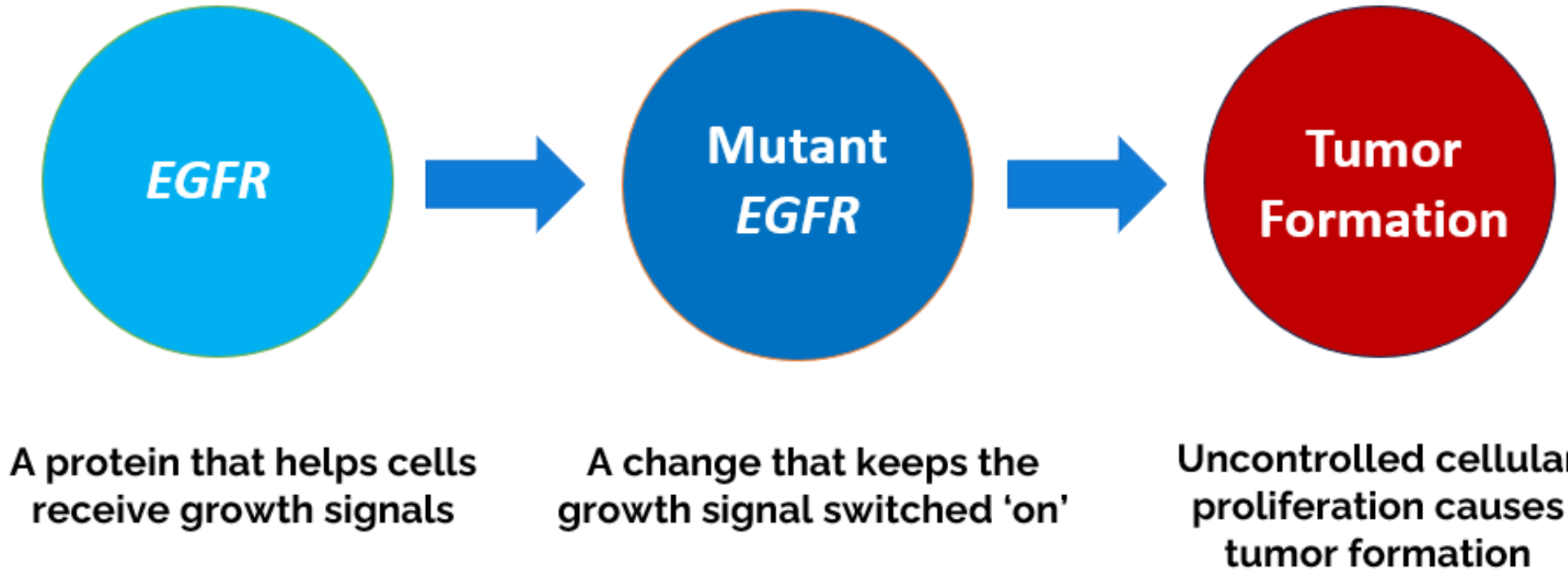
For Easier Viewing in PDF on Your Device

EGFR esisters

Module 1:
Understanding the Core Elements

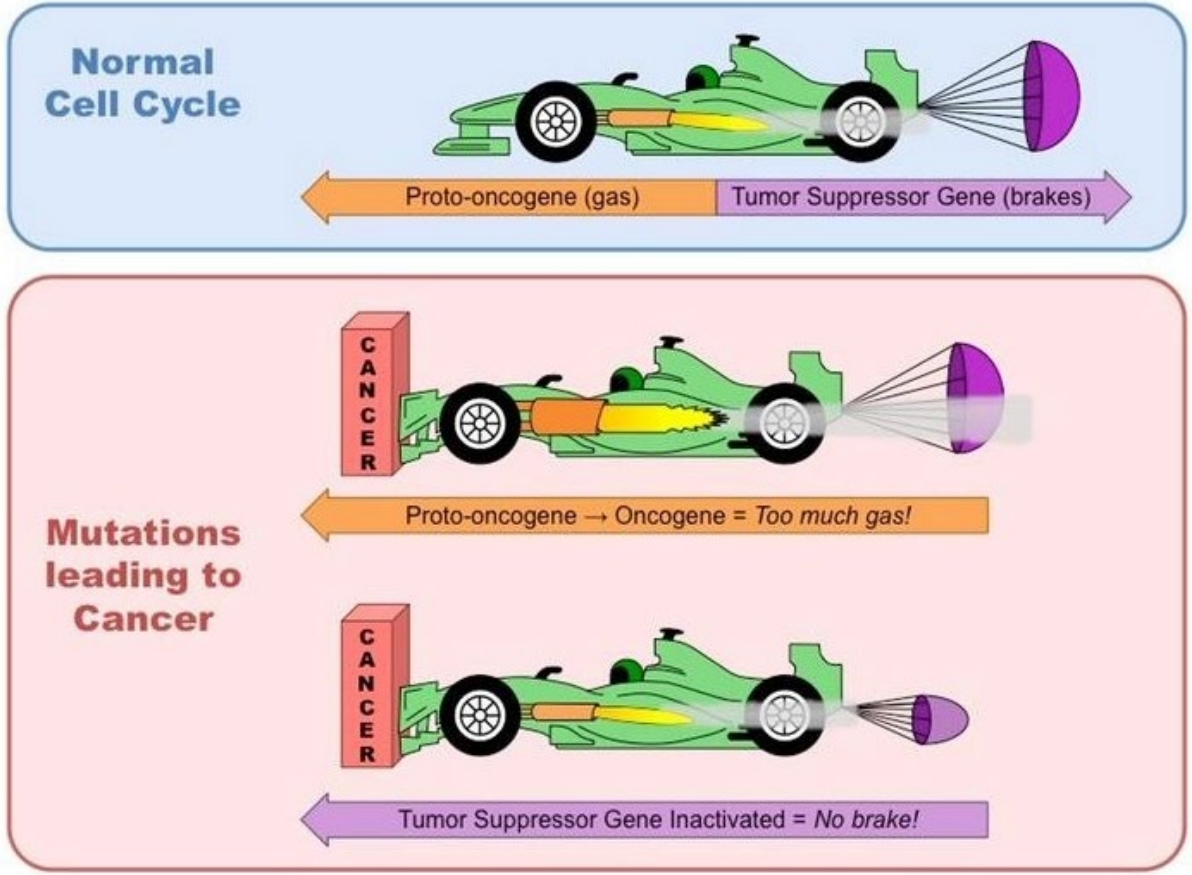
What Exactly is EGFR?

- *EGFR* is a gene that encodes the epidermal growth factor receptor (EGFR) protein



How do *EGFR* Mutations Cause Cancer?

- Consider the relationship of the brake pedal and gas pedal in a car
  - **Brakes** = tumor suppressor genes
    - Think *TP53*
  - **Gas** = oncogenes
    - Think *EGFR*
    - *EGFR* mutations give cells too much gas



What are the Types of *EGFR* Mutations?

Common *EGFR* mutations

Exon 19 deletions (~45-50%)
Exon 21 L858R point mutations (~35-40%)

EGFR Exon 20 Insertion

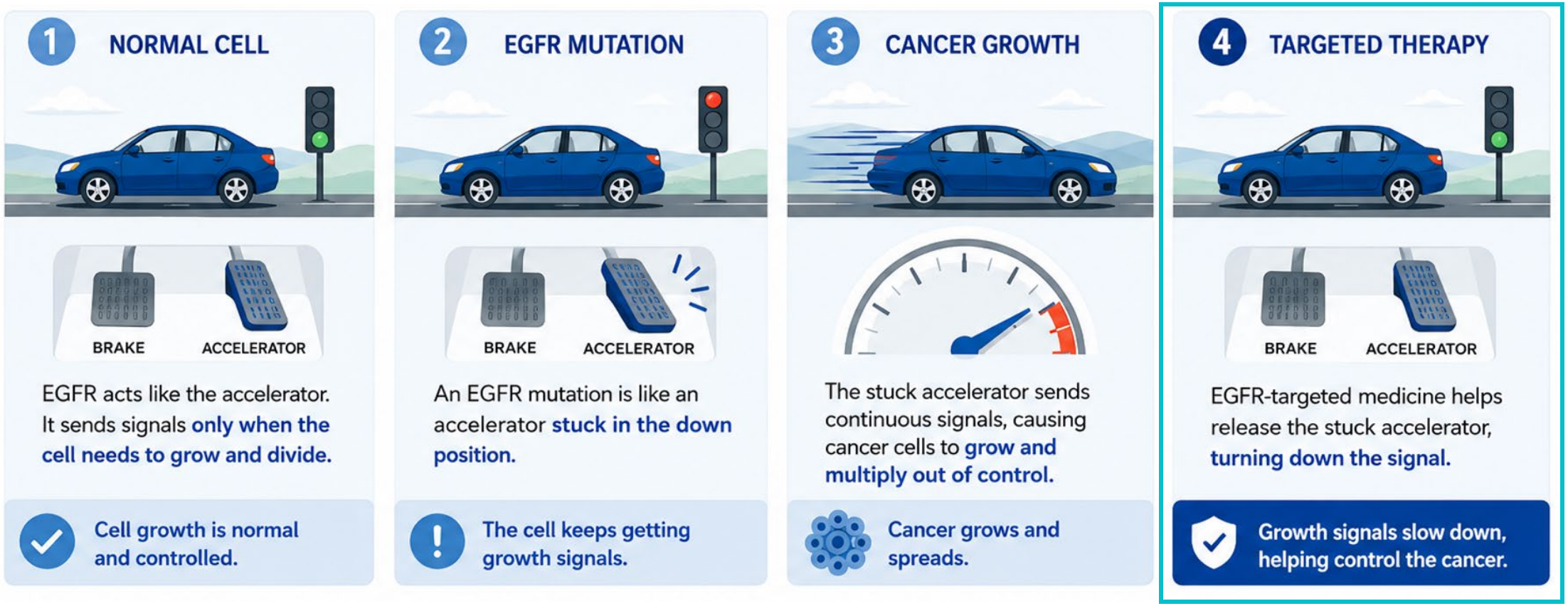
Exon 20 insertion – the most common of the uncommon (~4-12%)

Common Uncommon *EGFR* Mutations

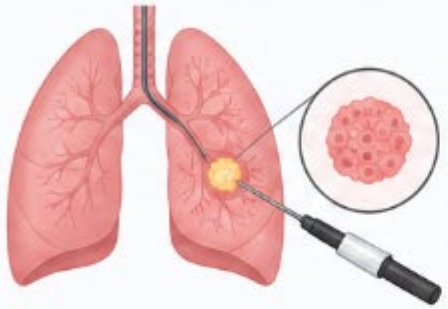
Exon 18, G719X, L861Q, S768I, E709X and L747X (all together = ~5-10%)

Why Do We Test for *EGFR* Mutations?

- Because *EGFR* is a *targetable mutation* – **testing informs treatment**

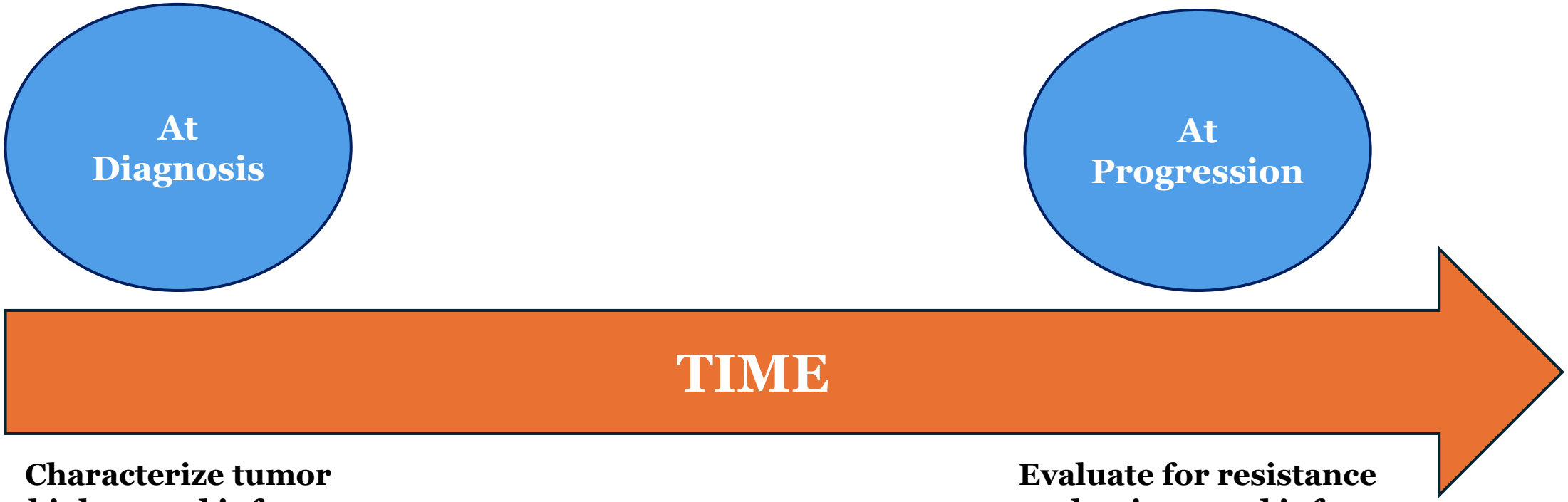


How Do We Test for Biomarkers?

	TISSUE BIOPSY Looks at a small piece of the tumor		LIQUID BIOPSY Looks at tumor DNA in the blood
WHAT IS IT?	 A sample is taken from the tumor through a procedure (bronchoscopy or needle biopsy).		 A simple blood draw is done. The test looks for pieces of tumor DNA (ctDNA) from the blood.
BENEFITS	**BENEFITS** • Provides a large amount of tumor tissue for detailed testing • Can detect many types of genetic changes • Considered the "gold standard"		**BENEFITS** • Minimally invasive – just a blood draw • Faster and easier to repeat • Can capture changes from different areas of the cancer
LIMITATIONS	**LIMITATIONS** • Invasive procedure; may cause discomfort or complications • May not be possible if the tumor is in a hard-to-reach area • Not always enough tissue for testing		**LIMITATIONS** • May not detect all *EGFR* mutations (especially if ctDNA is very low) • Less tissue, so some rare changes may be missed • May not be covered in all situations

NCCN Guidelines. NSCLC. Version 7.2026.

When Do We Test for Biomarkers?



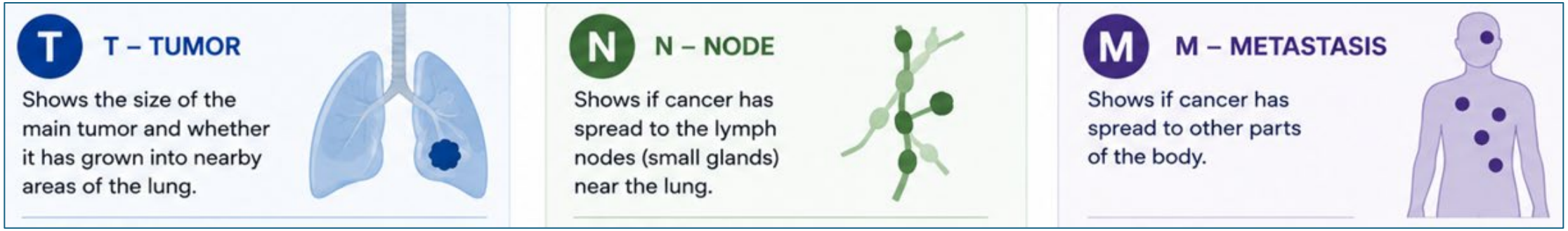
Module 2:
Screening, Staging, and Informing Treatment

What are the Stages of Lung Cancer?

- In essence, staging tells us where the cancer is located

The ABCs of TNM Staging

- The Tumor-Node-Metastasis (TNM) system gives us *more precise coordinates*

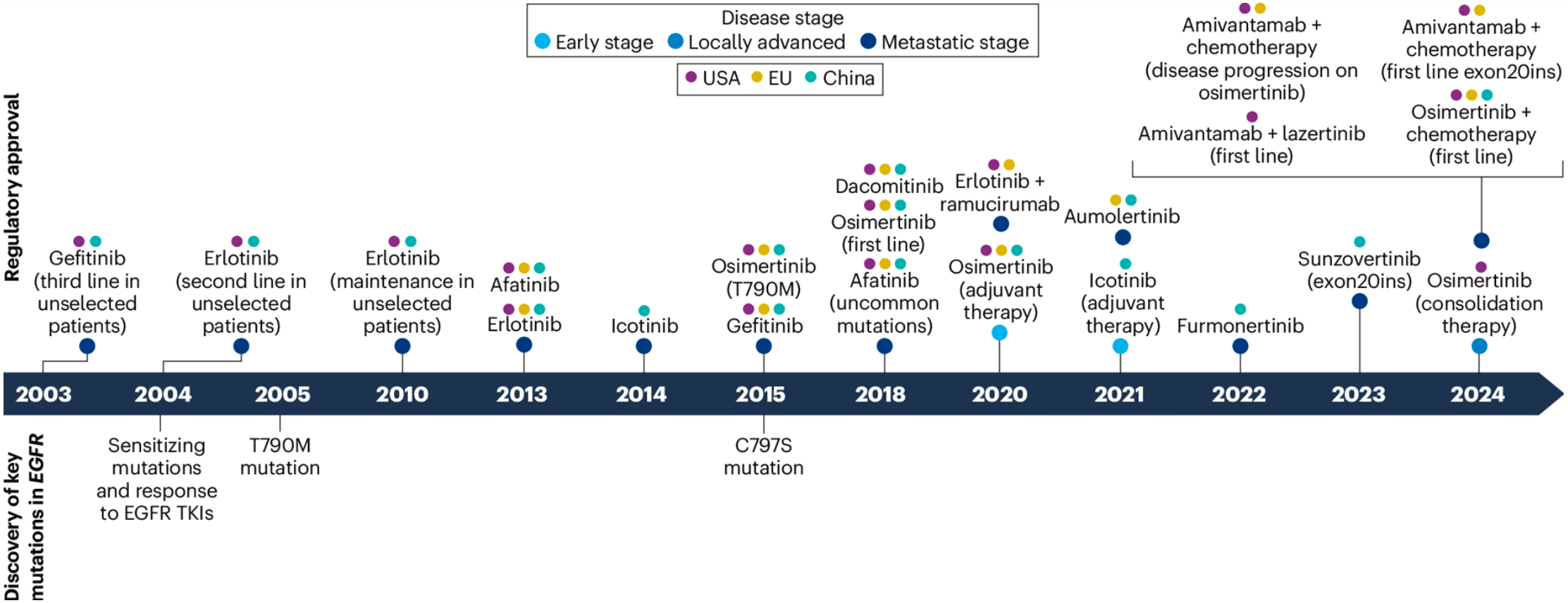


AJCC. TNM System. 9th Edition. 2025.

Module 3:
Best Practice Treatment of Stage IV EGFRm NSCLC

The Research Renaissance in *EGFR*

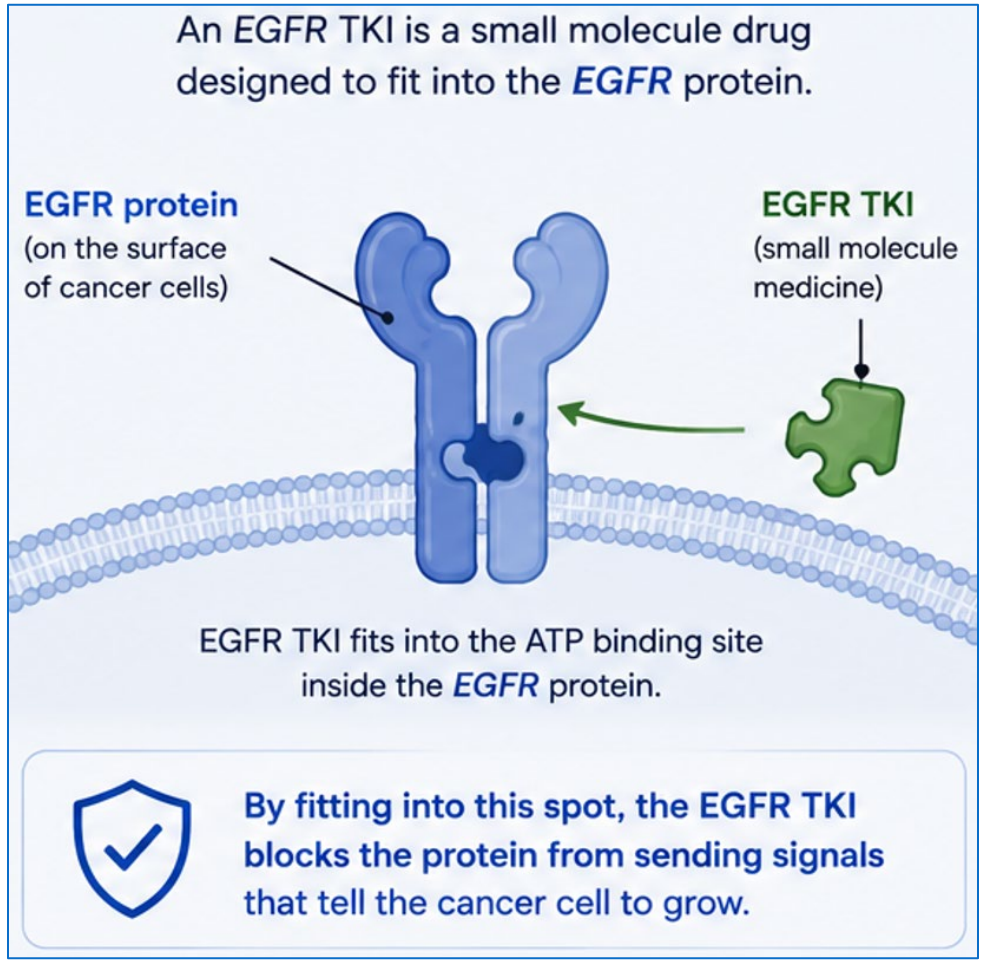
Staggering Drug Development Progress = ***Burgeoning Hope!***



Zhou F, et al. *Nat Rev Clin Oncol*. 2025.

EGFR Tyrosine Kinase Inhibitors (TKIs)

Blocking the Signals that Help Cancer Grow

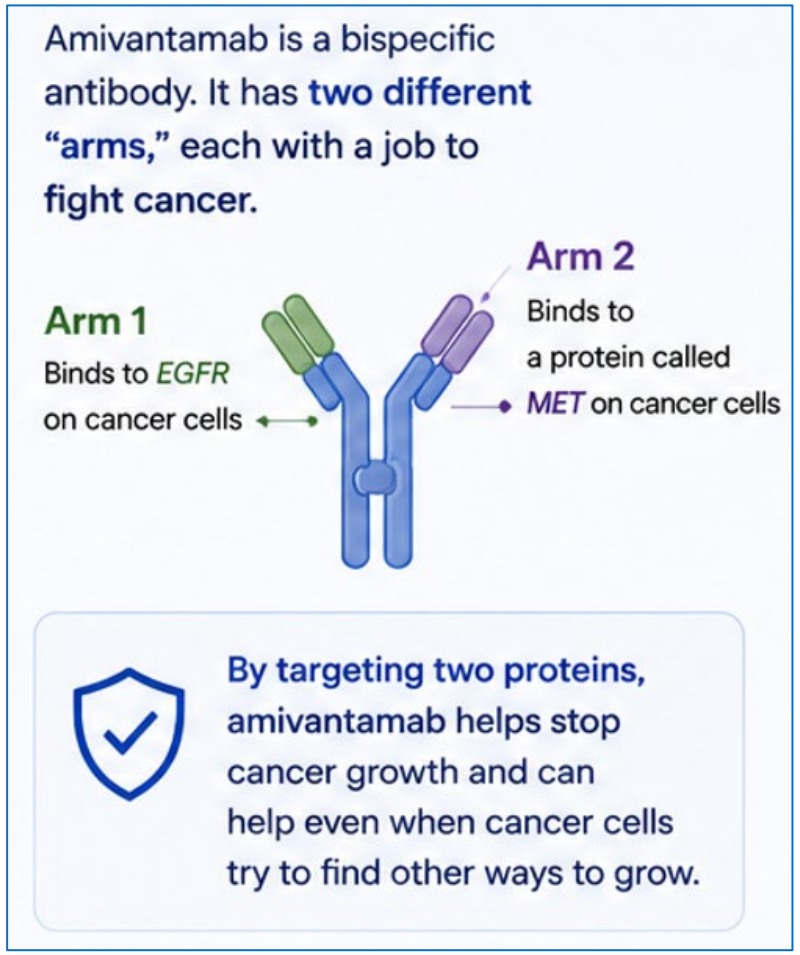


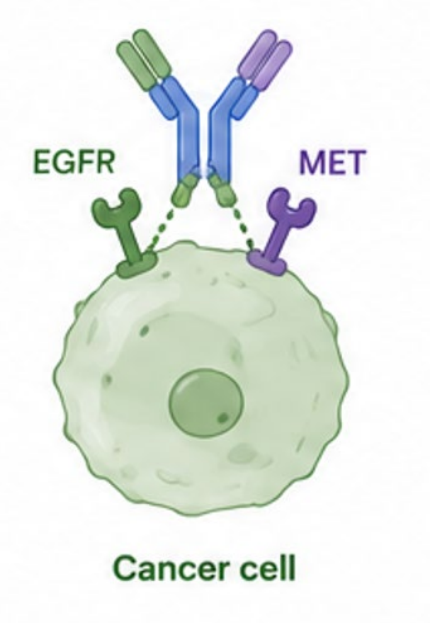
- *EGFR* TKI examples include:
  - Osimertinib
  - Lazertinib
  - Erlotinib
  - Gefitinib
  - Afatinib
  - Sunvozertinib
  - Others in development

FDA Prescribing Information; ClinicalTrials.gov.

Bispecific Antibodies (BsAbs)

Two Targets – One Medicine





- *Only 1 BsAb currently FDA-approved for EGFR+ lung cancer*
  - Amivantamab
  - Others in development

FDA Prescribing Information; ClinicalTrials.gov.

Antibody-Drug Conjugates (ADCs)

Delivering Treatment 'Directly' to Cancer Cells

What is datopotamab deruxtecan?

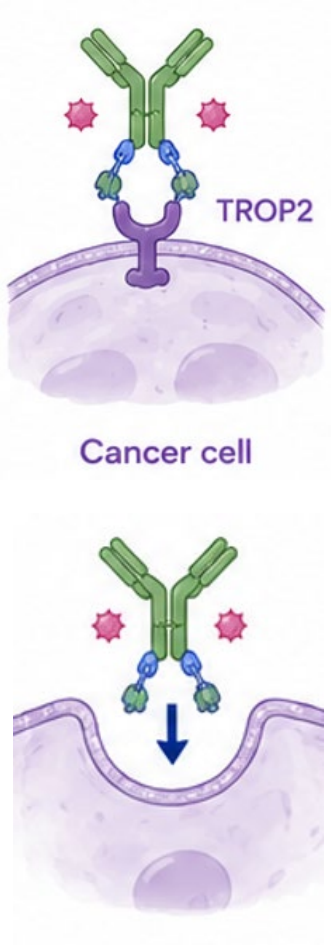
It is an ADC made of three parts:

Antibody (datopotamab)
Finds and attaches to *TROP2* on cancer cells

Linker
Acts like a safe "connector" that holds the drug

Chemotherapy (DXd)
A powerful medicine that kills cancer cells

This design helps deliver the medicine directly to cancer cells and limits harm to normal cells.



- *Only 1 ADC currently FDA-approved for EGFR+ lung cancer*
  - Datopotamab deruxtecan (Dato-DXd)
  - Others in development

FDA Prescribing Information; ClinicalTrials.gov.

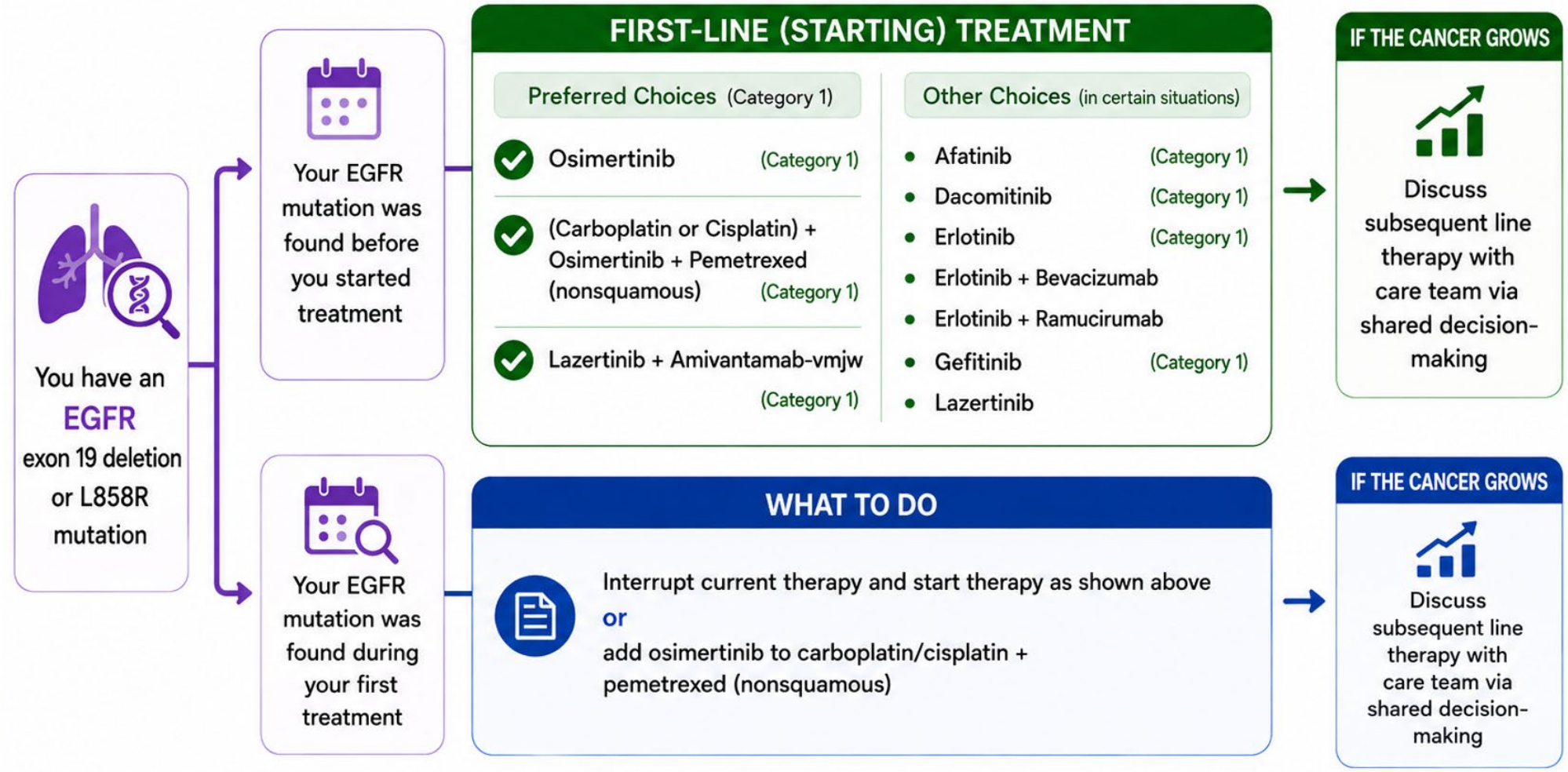
The Treatment Landscape Today

EGFR Exon 19 del or Exon 21 L858R-mutated Advanced or Metastatic Disease

First-Line

NCCN Recommendations

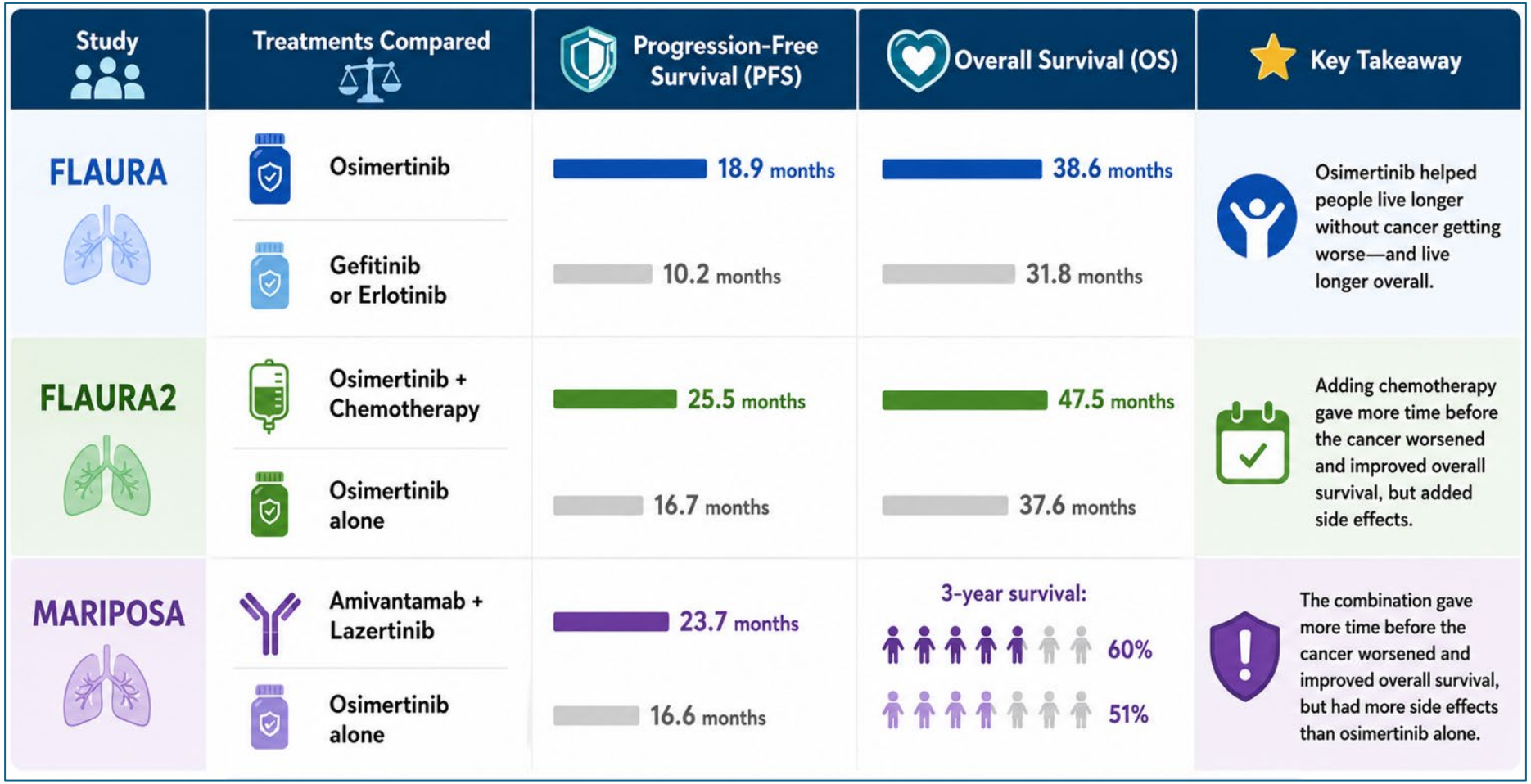
Version 7.2026 (August 7, 2026)



NCCN Guidelines. NSCLC. Version 7.2026.

Summary of Landmark 1L Trials

FLAURA, FLAURA2, and MARIPOSA



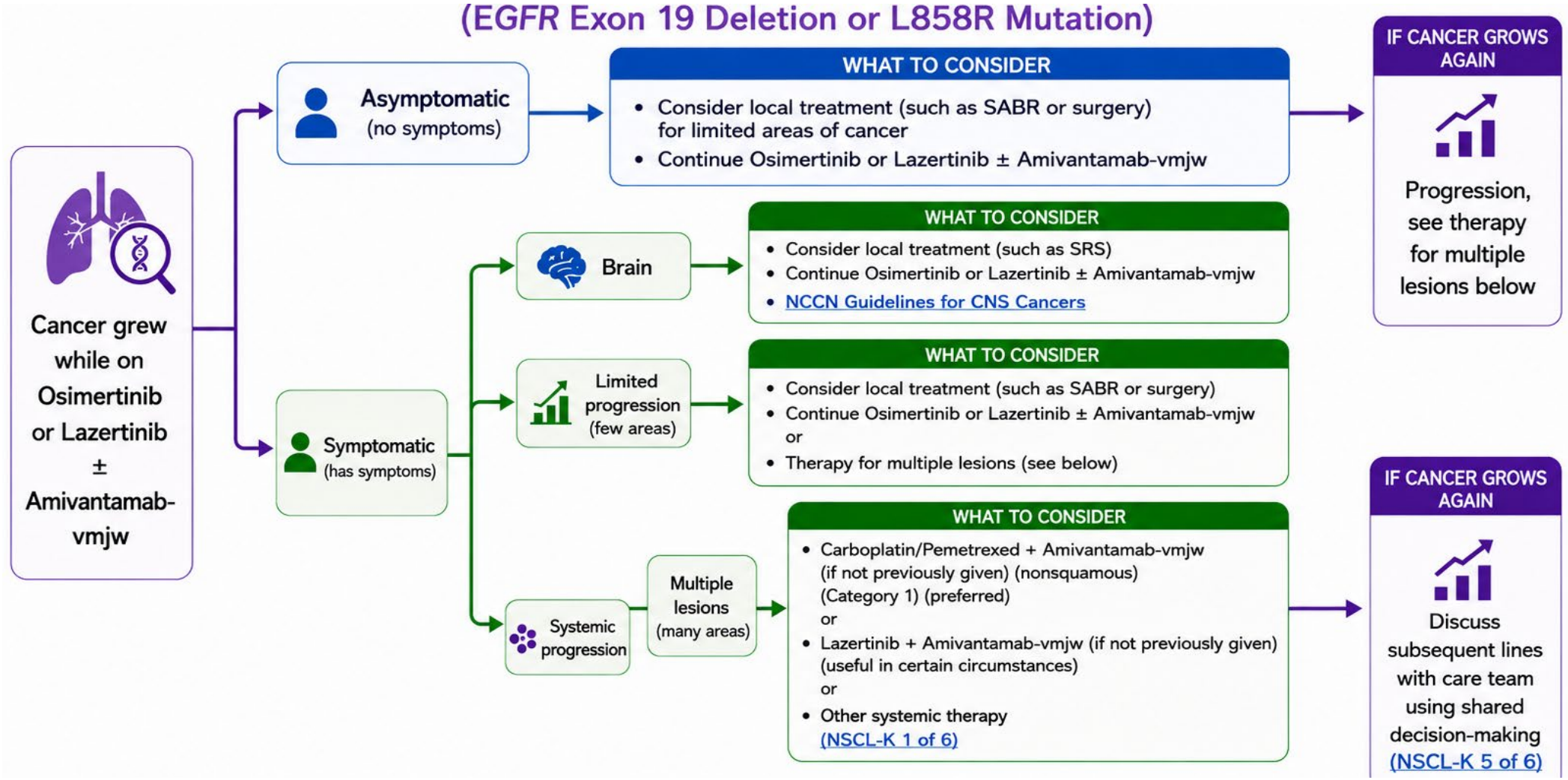
Soria J, et al. *N Engl J Med*. 2018; Ramalingam S, et al. *N Engl J Med*. 2020; Cho B, et al. *N Engl J Med*. 2024; Yang J, et al. *N Engl J Med*. 2025; Planchard D, et al. *N Engl J Med*. 2023; Janne P, et al. *N Engl J Med*. 2025.

EGFR Exon 19 del or Exon 21 L858R-mutated Advanced or Metastatic Disease

Subsequent-Line

NCCN Recommendations

Version 7.2026 (August 7, 2026)



NCCN Guidelines. NSCLC. Version 7.2026.

MARIPOSA-2

Amivantamab + Lazertinib + Chemo vs. Amivantamab + Chemo in 2L (post-osimertinib) EGFRm NSCLC

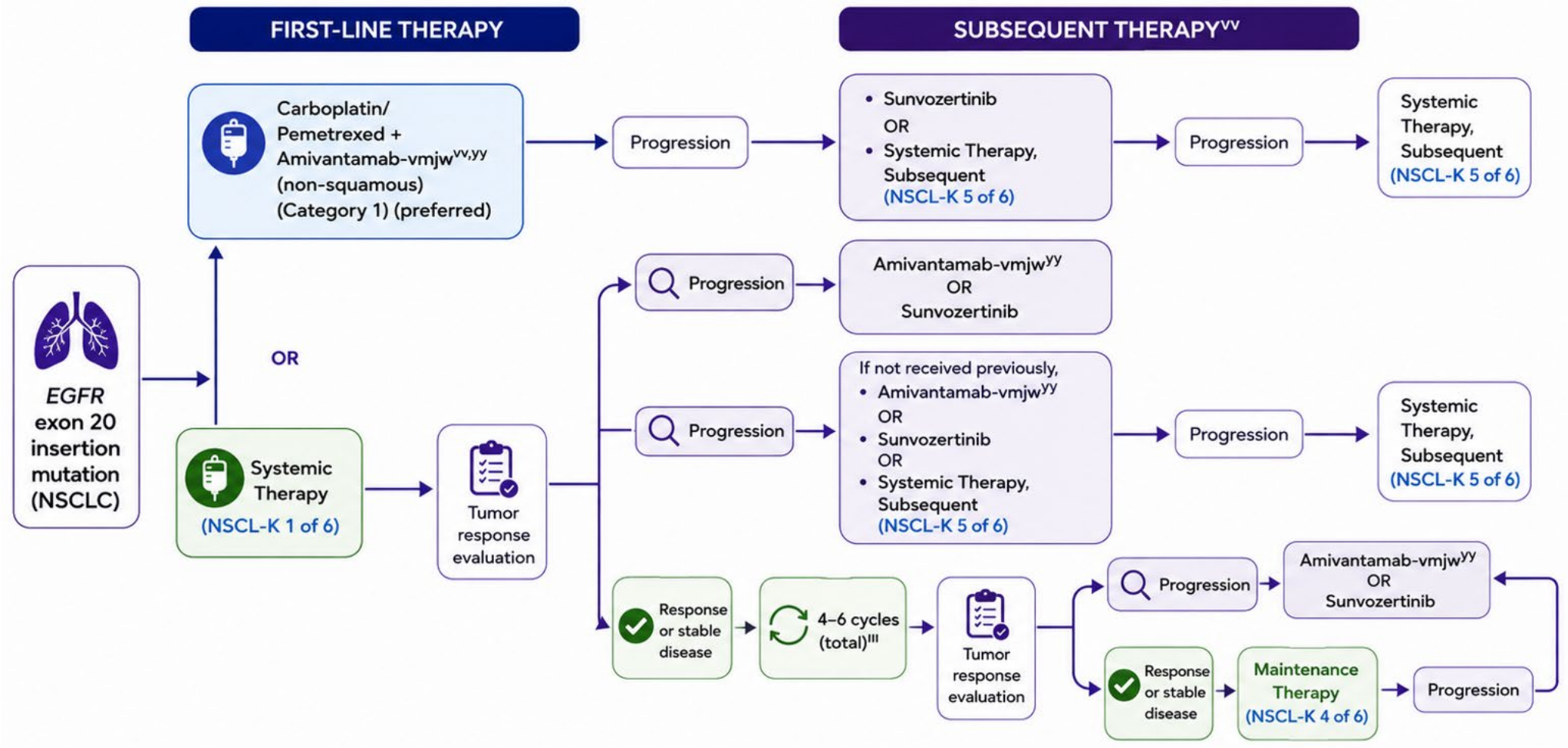
Results at a Glance	Amivantamab + Lazertinib + Chemo	Amivantamab + Chemo	Chemo alone
PFS Time before cancer worsened	8.3 months	6.3 months	4.2 months
Intracranial PFS Time before cancer worsened in the brain	12.8 months	12.5 months	8.3 months
Overall response rate Patients whose tumors shrank	63%	64%	36%
Grade 3+ side effects More serious side effects	92%	72%	48%

Passaro A, et al. *Ann Oncol*. 2024.

EGFR Exon 20 Insertion Advanced or Metastatic Disease

NCCN Recommendations

Version 7.2026 (August 7, 2026)



NCCN Guidelines. NSCLC. Version 7.2026.

Summary of Exon 20 Trials

PAPILLON, WU-KONG1B

PAPILLON — first-line treatment

308 patients | Amivantamab + chemo vs chemo alone

RESULT	Amivantamab + Chemo		Chemo alone
Time before cancer worsened (PFS)	11.4 months	vs	6.7 months
Tumor response (ORR)	73%	vs	47%
Serious/high-grade side effects (Grade ≥3)	75%	vs	54%
Serious adverse events	37%	vs	31%

WU-KONG1 — after platinum chemotherapy

174 randomized patients | Sunvozertinib 200 mg vs 300 mg once daily

RESULT	Sunvozertinib 200 mg		Sunvozertinib 300 mg
Tumor response (confirmed ORR)	45.9%	vs	47.2%
How long response lasted (median DoR)	11.1 months	vs	13.8 months
Grade ≥3 diarrhea	2.2%	vs	18%
Grade ≥3 increased CPK*	6.6%	vs	12.6%

Zhou C, et al. *N Engl J Med*. 2023; Sanborn R, et al. *Target Oncol*. 2025; Yang J, et al. *J Clin Oncol*. 2025.

Module 4:
Best Practice Treatment of Earlier Stage EGFRm NSCLC

Treating Earlier Stage *EGFR*+ NSCLC

Resectable Disease (surgery is an option)

- **Neoadjuvant therapy** = treatment *prior to surgery*
- **Adjuvant therapy** = treatment *after surgery*

Unresectable Disease (surgery is not an option)

- **Consolidation therapy** = treatment used to maintain therapeutic benefit/reduce recurrence risk in stage III disease *after platinum-based chemoradiotherapy (CRT)*

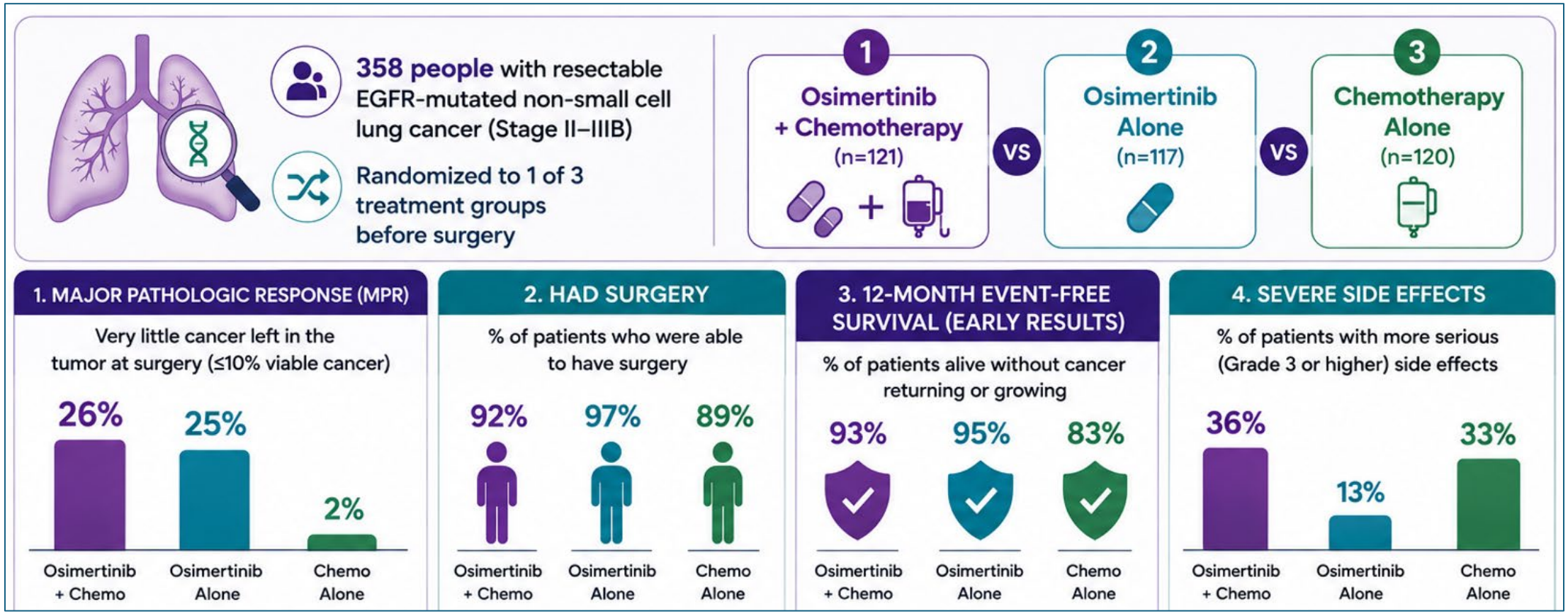
The Treatment Landscape Today

Resectable Disease

Neoadjuvant

NeoADAURA

Osimertinib Prior to Surgery



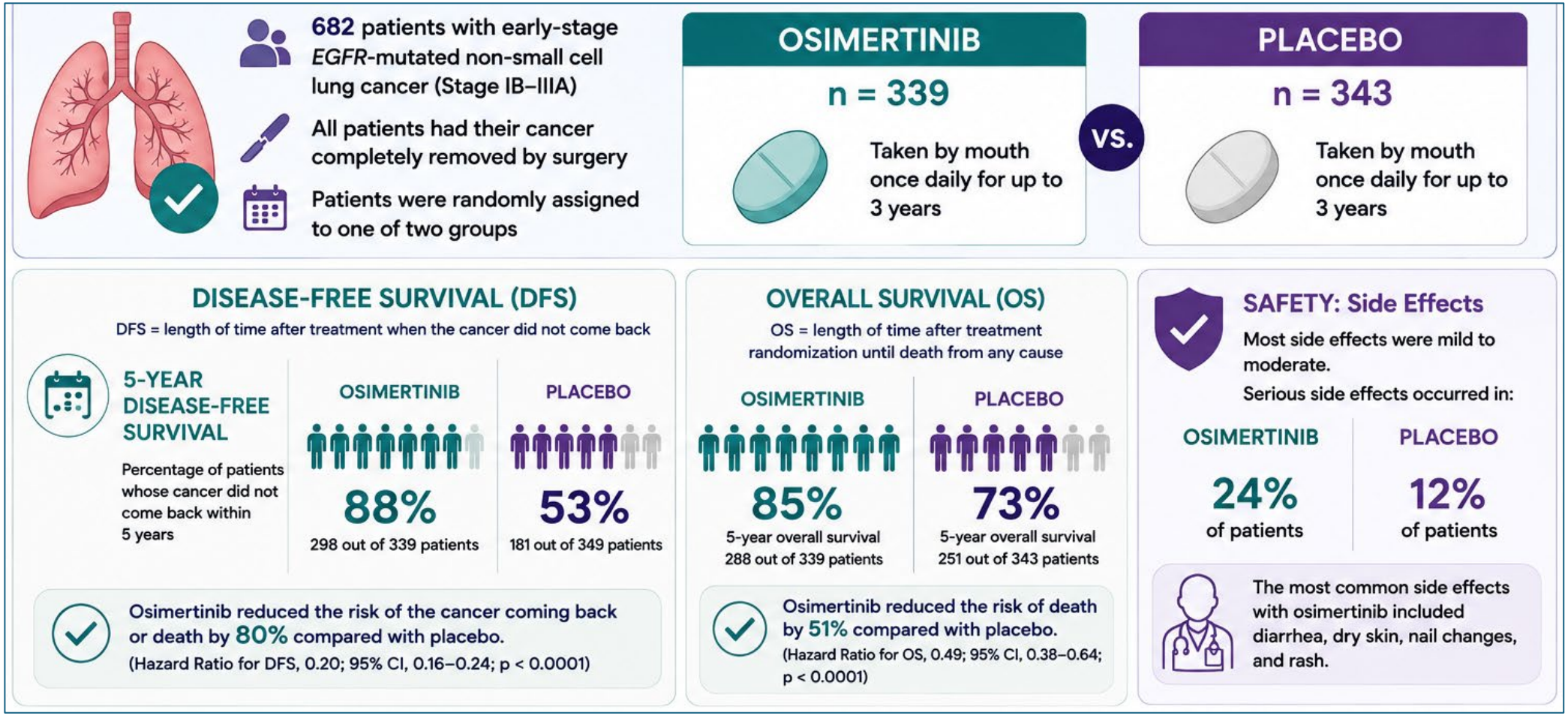
He J, et al. *J Clin Oncol*. 2025.

Resectable Disease

Adjuvant

ADAURA

Osimertinib After Surgery



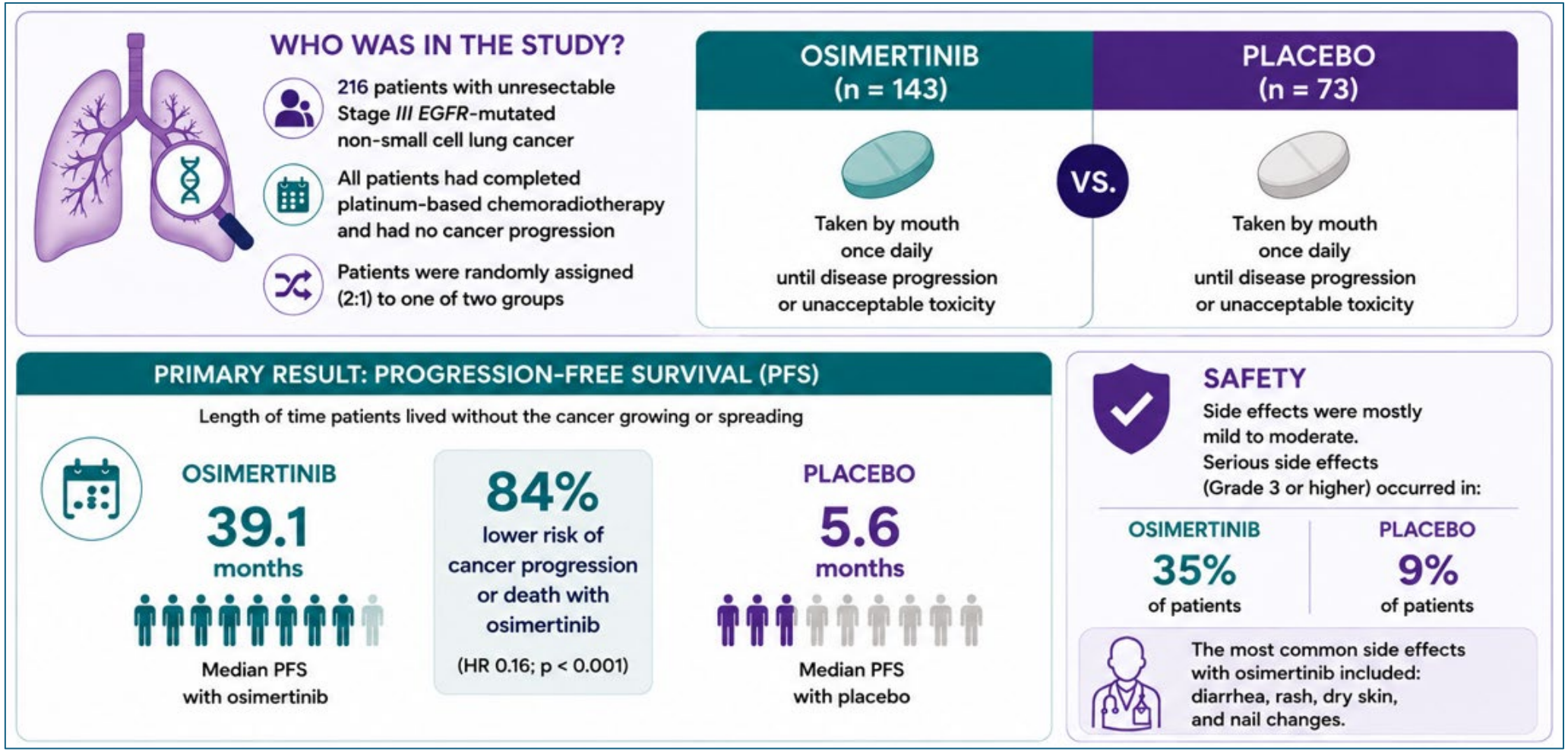
Wu Y, et al. *N Engl J Med*. 2020; Tsuboi M, et al. *N Engl J Med*. 2023.

Unresectable Disease

Consolidation

LAURA

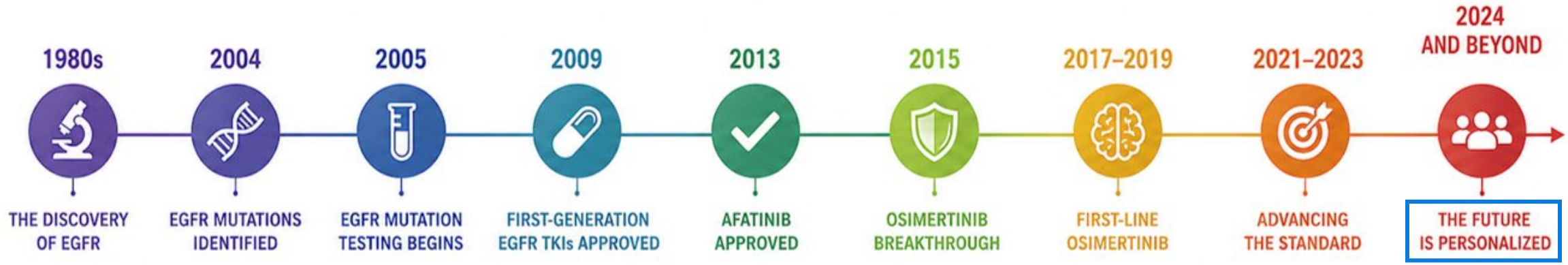
Osimertinib After Chemoradiotherapy (CRT)



Lu S, et al. *N Engl J Med*. 2024; Ramalingam S, et al. *J Thoracic Onc*. 2025.

Module 5:
We've Come a Long Way – Where to Next?

The Future is Bright (*and Personal!*)



Ongoing Momentum and Innovation

- Next-generation EGFR TKIs
  - Numerous "4th-generation" agents in early-phase clinical trials
  - Zipalertinib under FDA review for 2L+ *EGFR* exon20 - ***FDA PDUFA date = February 2027***
    - + *positive 1L readout this past week!*
- Antibody-Drug Conjugates
  - Sacituzumab tirumotecan demonstrated survival benefit vs. docetaxel in previously treated (post-TKI) advanced *EGFR*m NSCLC - ***Granted FDA Breakthrough Therapy Designation***
- Bispecific Antibodies
  - Ivonescimab has demonstrated PFS benefit when combined with platinum doublet chemo vs. chemo alone in 2L+ (post-TKI) advanced *EGFR*m NSCLC - ***FDA PDUFA date = November 2026***
- ***Smarter combination therapies***
- ***More "personalized" treatment***

Su C, et al. *Transl Cancer Res*. 2025; Piotrowska Z, et al. *J Clin Oncol*. 2025; Heymach J, et al. *Future Oncol*. 2025; Fang W, et al. *N Engl J Med*. 2026; Fang W, et al. *JAMA*. 2026; ClinicalTrials.gov.

Interactive Q & A