

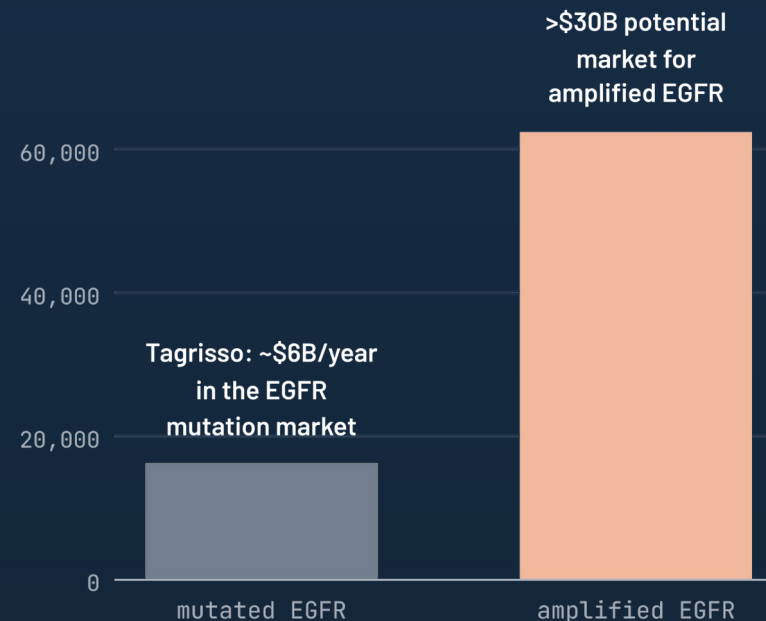
THE SECOND ACT OF EGFR

Lessons from what patient data reveals about drug programs



by Pawel Zawadzki, PhD

No. of patients with EGFR alteration
in the US (5 tissues)



\$36B+

Cumulative revenue generated by EGFR inhibitor Tagrisso (osimertinib)



THE EXPECTED **SUCCESS STORY**

EGFR is one of the most powerful oncogenes, and it represents a beautiful success story of precision oncology.

Is a new gold rush about to start in the EGFR space?

Patient data shows the EGFR market could be massively expanded.

WHAT THE PATIENT DATA REVEALED

EGFR is a great drug target.

- Activating *EGFR* mutations are well understood and Tagrisso has won that market, currently generating ~\$6B/year.
- But there are 5× more patients with amplified *EGFR* compared to ones activated by mutations.
- Monoclonal antibodies targeting EGFR delivered clinical benefits, yet they never reached the potential proportional to the size of the market.

EGFR alterations across tissues

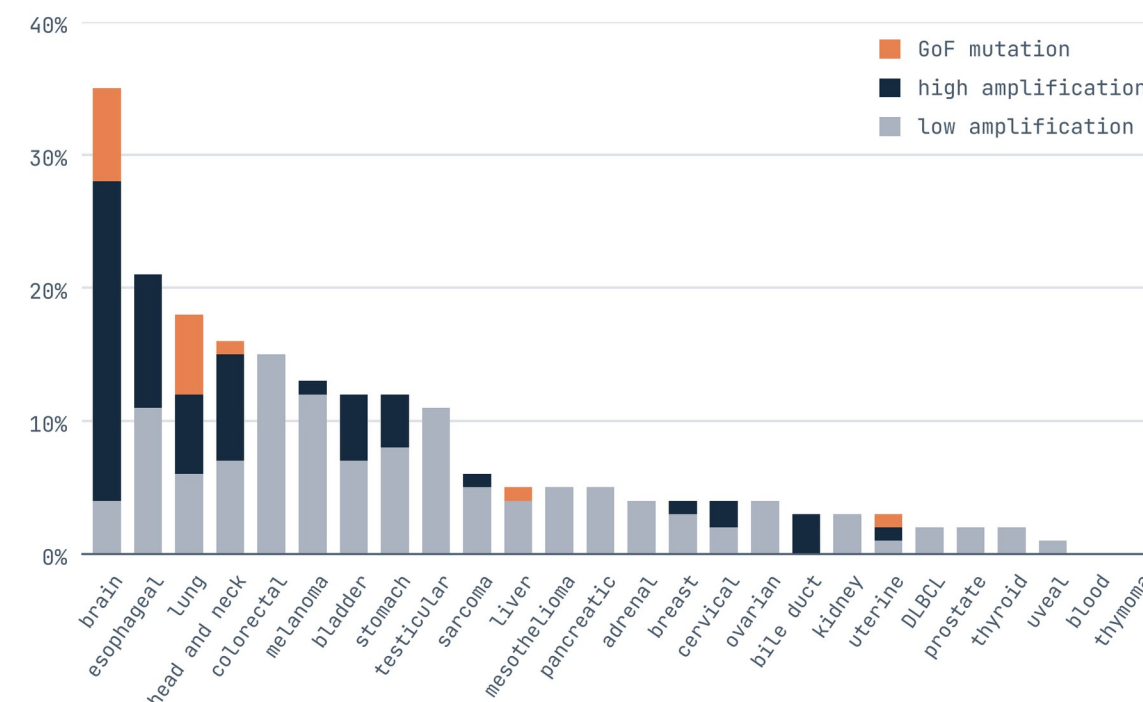


Figure 1. GoF (Gain-of-Function) mutation; high amplification (≥ 7 additional *EGFR* gene copies); low amplification (2–6 additional gene copies).

WHAT THE **PATIENT DATA** REVEALED

The comparison of mutated to amplified EGFR patients, revealed that amplified EGFR is not a solo-driver.

- mAbs targeting EGFR were expected to match Tagrisso, yet they underperformed as amplified EGFR is a team player.
- The concept of amplified EGFR being a team player is being validated by EGFR-MET and EGFR-LGR5 bispecific antibodies.
- The big question is: which product will win the EGFR amplified market?

Mutated vs amplified EGFR

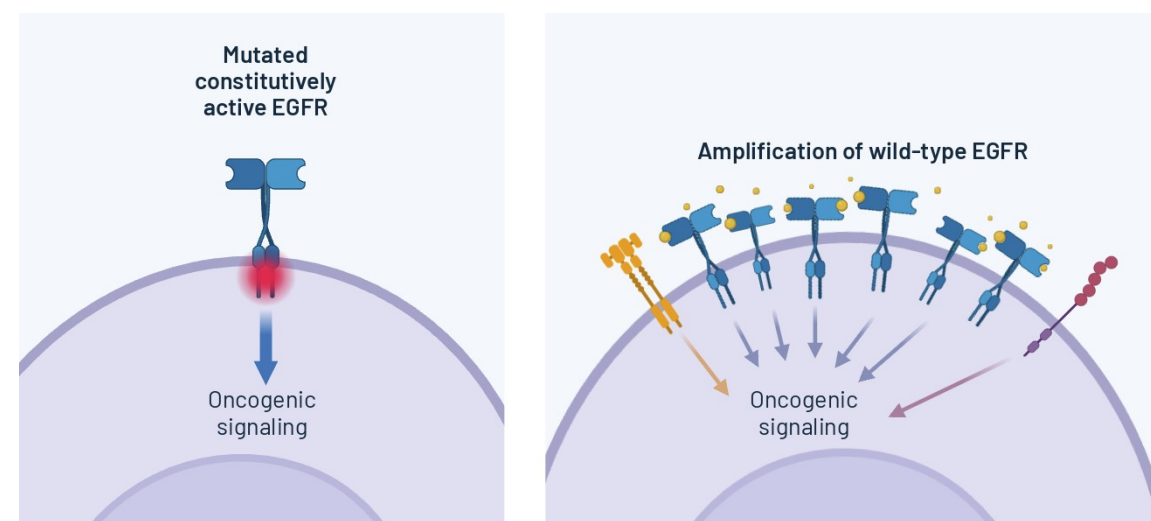


Figure 2. In lung cancer, mutated EGFR is a solo driver, while amplified EGFR requires supercharging by other players.

THE TAKE-HOME MESSAGE

EGFR AMPLIFICATIONS = OPPORTUNITY



Mutation vs amplification

Patient data confirms the extreme addiction of tumors to EGFR. But mutation $\neq$ amplification, explaining the underperformance of monoclonal antibodies and suggesting that BiAb might have a massive impact in the space.

EGFR needs supercharging

BiAb can exploit the mechanisms used by tumors to supercharge EGFR signalling. EGFR-MET is a validation of what was obvious, but patient data suggest that the EGFR-MET product will not win this space.



STRATEGIC RECOMMENDATIONS

FROM INSIGHT TO ACTION

CONSULT PATIENT DATA FOR **RELIABLE OUTCOMES**

01

Mutated EGFR is such a strong driver

Therefore, no other supercharging is required.

02

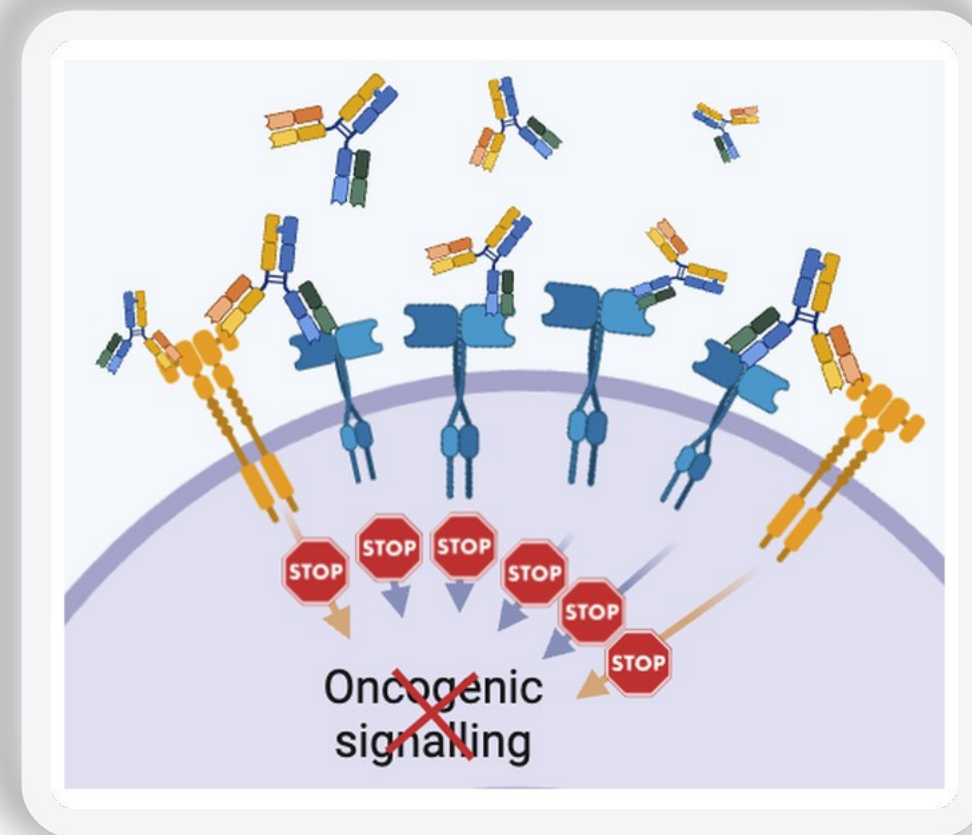
Mutation $\neq$ amplification

In patient data, you can measure what other drivers are co-activated when *EGFR* gets amplified.

03

Patient data informs BiAbs design and winning strategy

Select highly amplified (>7 additional *EGFR* copies) patients for your initial trials to maximize the therapeutic window. Then, from patient biopsy data, select the second target to win the space.





**Medicines intended to work in patients should
be developed with patient data in mind.**

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