

Before You Invest:

Lessons From What Patient Data Reveals About Drug Programs

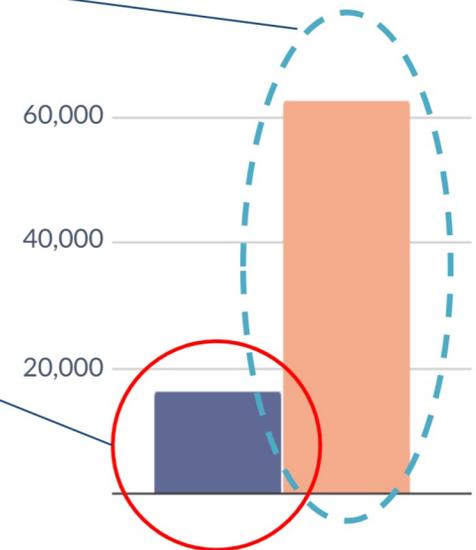


by Pawel Zawadzki, PhD

The second act of EGFR

>\$30B potential market
for amplified EGFR

Tagrisso: ~\$6B/year in the
EGFR mutation market



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?

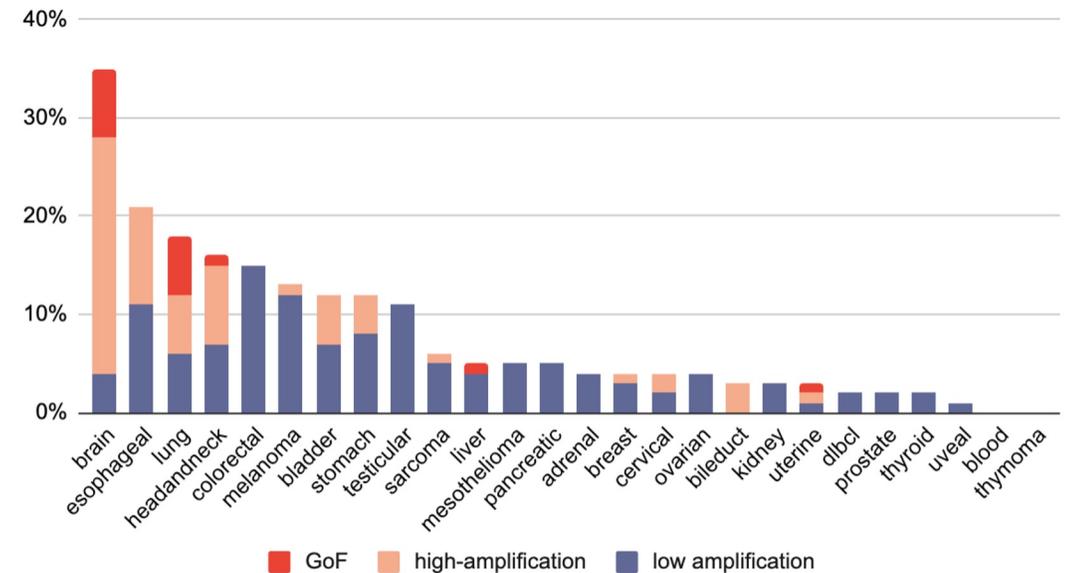
Patient data shows the EGFR market could be massively expanded.

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 5x 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



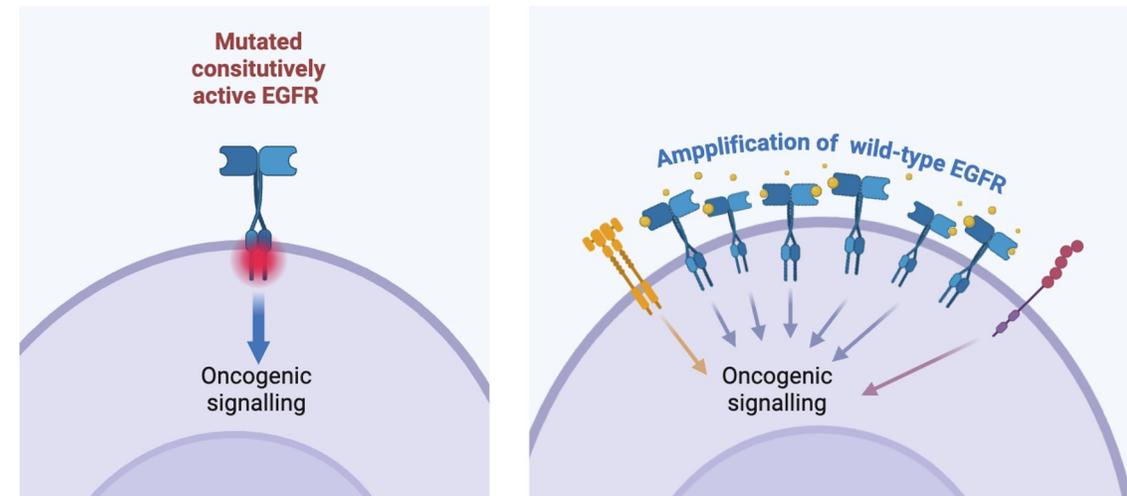
GoF (Gain-of-Function) mutation; high amplification (≥ 7 additional EGFR gene copies); low amplification (2-6 additional gene copies).

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



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:



Mutated EGFR is such a strong driver

Therefore, no other supercharging is required.



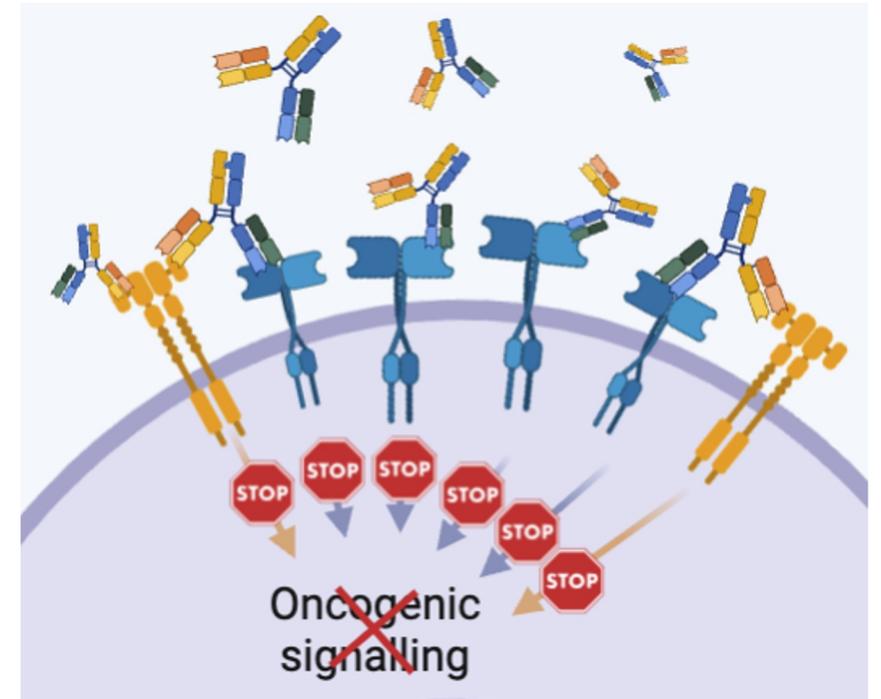
Mutation \neq amplification

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



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.**

For inspirations check:

<https://www.gordion.bio/before-you-invest>