EGFRChannel | OncLive

EGFR PACC Mutations Define a Distinct NSCLC Subclass With Growing Treatment Options

Distinct *EGFR* Subclass With Expanding Targeted Treatment Options

What to Know

***EGFR* PACC mutations account for:**

12%
of all *EGFR* mutations

1.5-2x
More common than *EGFR* exon 20 insertions

What makes PACC mutations unique?

- Located near the *EGFR* drug-binding pocket
- Frequently occur as compound mutations
- Show reduced sensitivity to first- and third-generation *EGFR* TKIs
- Emerging as a distinct molecular subtype requiring tailored treatment

Additional Clinical Insight

Afatinib improved:

- Progression-free survival (PFS); Objective response rate (ORR) vs platinum-doublet chemotherapy in patients with uncommon *EGFR* mutations.

Looking Ahead

Molecular testing is evolving to:

- Better classify PACC mutations;
- Predict sensitivity to *EGFR* TKIs;
- Guide more personalized treatment decisions.

Key Highlights

12%
of all *EGFR* mutations are PACC

Amivantamab + lazertinib
41 Months
Median overall survival

Silevertinib
60% ORR

Firmonertinib
68.2% ORR
100% DCR

Therapy	ORR	PFS	DCR*
Silevertinib	60%	15.2	91%
Firmonertinib	68.2%	16.0	100%
Enozertinib	36%		91%
Amivantamab + Lazertinib	57%	19.5	

Doherty K. OncLive. Accessed July 30, 2026. https://www.onclive.com/view/egfr-pacc-mutations-define-a-distinct-nsclc-subclass-with-growing-treatment-options

*DCR, disease control rate.