

ALPACCA: Ph3 trial of firmonertinib vs investigator's choice of EGFRi as 1L treatment for locally advanced or mNSCLC with EGFR PACC mutations

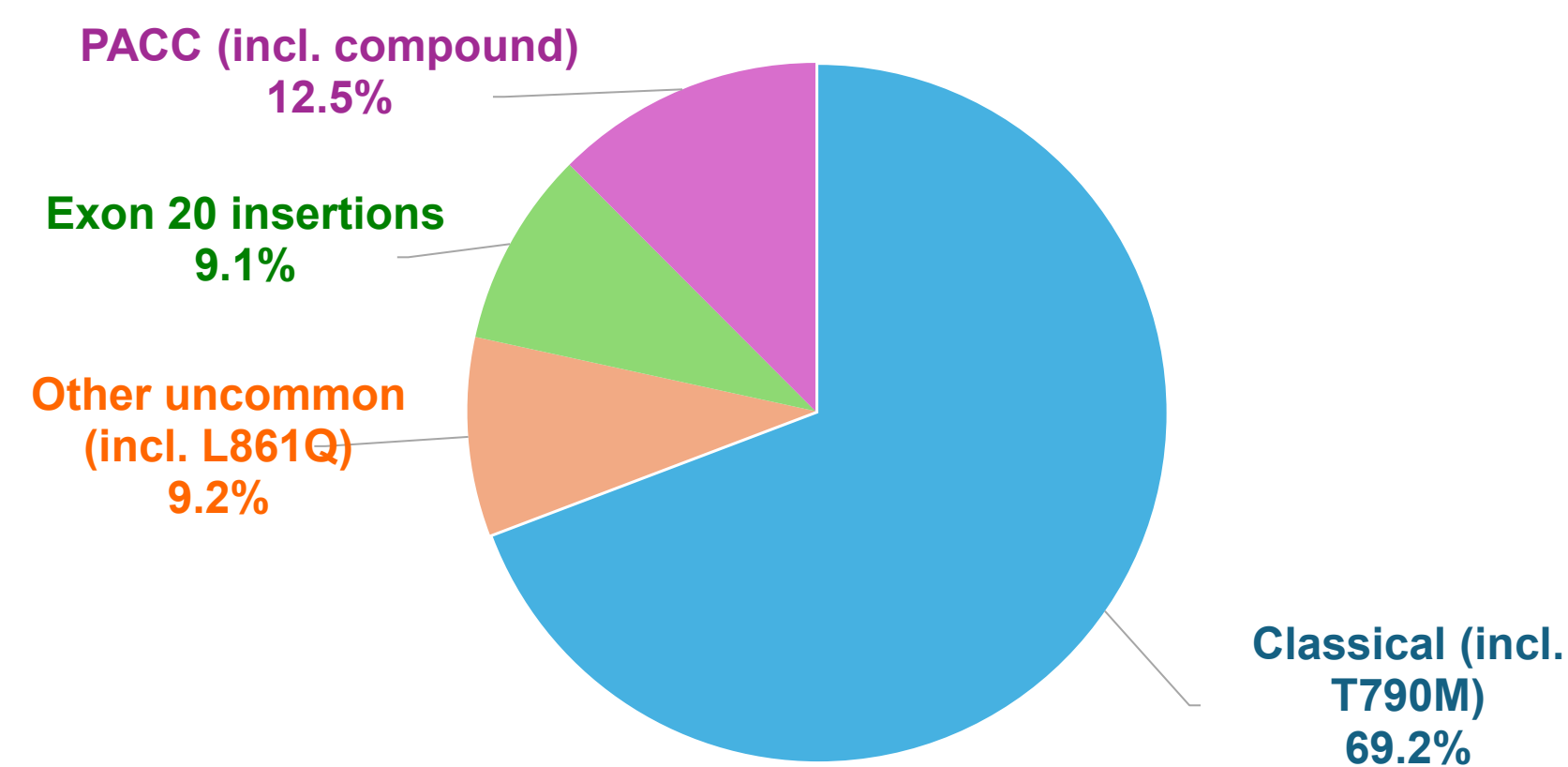
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INTRODUCTION

- PACC mutations are a subset of uncommon EGFR activating mutations predicted to alter the orientation of the P-loop and/or alpha C-helix domains, which span exons 18 through 21.
 - PACC mutations may occur as single or compound mutations.
 - Examples of PACC mutations include G719X, S768I, E709X, E709_T710delinsD, V769X, L747X, & R776X.
- PACC mutations comprise approximately 12.5% of all NSCLC EGFR mutations^{a,b}.

Figure 1. Distribution of EGFR Mutation



- There is no globally accepted standard-of-care treatment for patients with EGFR uncommon mutations including PACC mutations.
 - Treatment options include EGFR tyrosine kinase inhibitors (TKIs), such as osimertinib and afatinib, or chemotherapy.
- Firmonertinib is a once daily, oral, highly brain-penetrant, EGFR TKI that targets classical and uncommon EGFR mutations^c.
- In the phase 1b FURMO-002 study (FURTHER), first-line locally advanced or metastatic EGFR PACC mutation NSCLC patients treated with firmonertinib 240 mg daily had promising systemic antitumor activity (n=22)^d. See table 1.
- Firmonertinib was generally well-tolerated, with manageable EGFR TKI-associated adverse events, and low drug discontinuation rates.

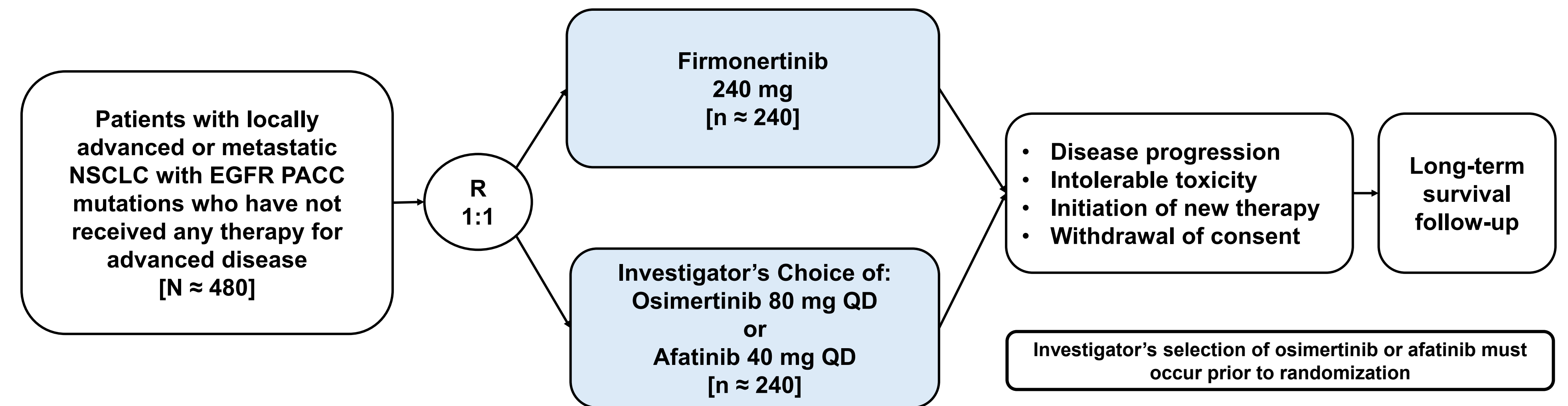
Table 1. PACC Cohort: Efficacy Outcomes by BICR for 1L Patients

	240 mg QD n=22
Best ORR, % (95% CI) ^a	81.8% (59.7–94.8)
Confirmed ORR, % (95% CI)	68.2% (45.1–86.1)
Best overall response, n (%)	
Complete response (CR)	0 (0%)
Partial response (PR)	15 (68.2%)
Stable disease (SD)	7 (31.8%)
Progressive disease (PD)	0 (0%)
Median Duration of Response, months	14.6
DCR (CR+PR+SD), % (95% CI)	100% (84.6% – 100%)

^aIncludes confirmed and unconfirmed responses. Data from Le et al, WCLC 2025.

METHODS

Figure 2: ALPACCA Study Design



Primary Endpoint: PFS and ORR per RECIST v1.1 by BICR

Secondary Endpoints: OS, PFS and ORR by investigator, DoR, PFS2, Safety and Tolerability

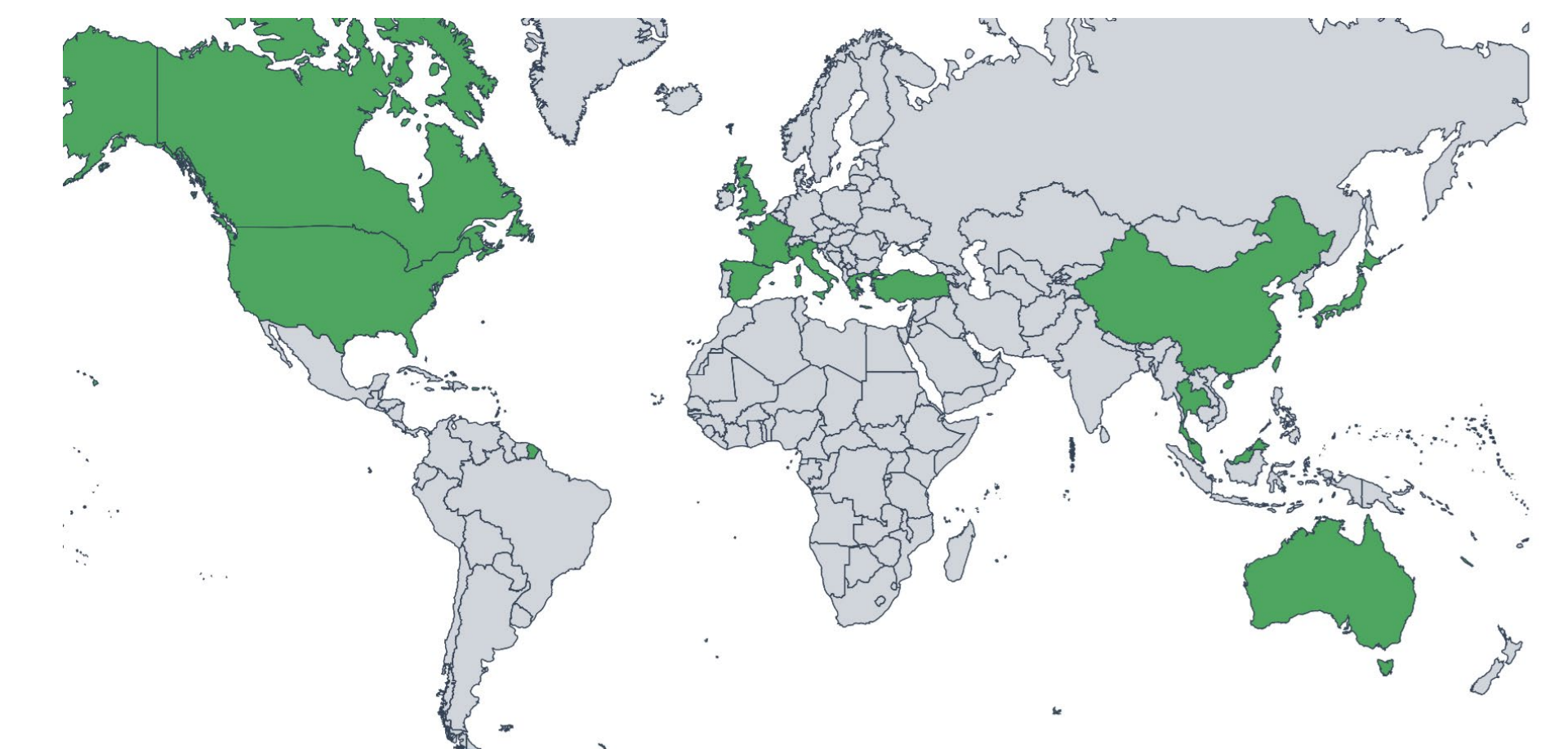
Table 2: Key Inclusion Criteria

- Histologically or cytologically documented, locally advanced or metastatic NSCLC not amenable to curative surgery or radiotherapy
- Documented results of the presence of an EGFR PACC mutation in tumor tissue or blood from local testing
- No prior systemic anticancer therapy regimens received for locally advanced or metastatic NSCLC, including prior treatment with any EGFR targeting agents (e.g., previous EGFR TKIs, monoclonal antibodies, or bispecific antibodies)
- Patients who have received prior neo-adjuvant and/or adjuvant chemotherapy, immunotherapy, or chemo radiotherapy for non-metastatic disease must have experienced a treatment free interval of at least 12 months
- Patients with asymptomatic central nervous system (CNS) metastases are eligible

Table 3: Key Exclusion Criteria

- Prior systemic anticancer therapy in the locally advanced or metastatic setting
- Prior EGFR TKI therapy

Figure 3: ALPACCA Participating Countries (enrollment ongoing)



- 17 countries, 150 sites
 - Australia, Canada, China, France, Greece, Hong Kong, Italy, Japan, Malaysia, Singapore, South Korea, Spain, Taiwan, Thailand, Turkey, United Kingdom, United States

REFERENCES & ACKNOWLEDGEMENTS

^aRobichaux JP, Le X, Vijayan RSK, et al. Structure-based classification predicts drug response in EGFR-mutant NSCLC. *Nature*. 2021;597(7878):732–7.

^bNilsson MB, Mounir Z, Musib L, et al. Firmonertinib (furmonertinib) is a highly brain-penetrant EGFR inhibitor broadly active against uncommon EGFR mutations, including PACC and exon 20 insertions. Poster presented at: American Association for Cancer Research (AACR) Annual Meeting; April 05–10, 2024; San Diego, CA.

^cMusib et al. Furmonertinib is an oral, irreversible, highly brain-penetrant pan-EGFR mutant inhibitor with activity against classical and atypical EGFR mutations. NACLC 2026.

^dLe et al. Final analysis of firmonertinib monotherapy data from Ph 1b study in EGFR PACC mutant NSCLC presented. WCLC 2025.