# FURVENT: Global, Phase 3 Trial Testing Firmonertinib (Furmonertinib) versus Chemotherapy as First-Line Treatment for Advanced NSCLC with EGFR Exon 20 Insertion Mutations

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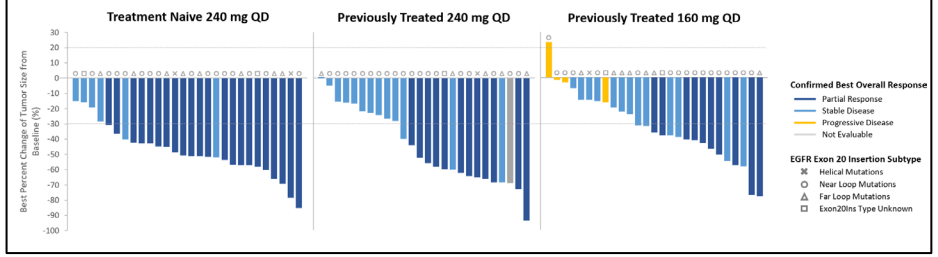
## Background

- Firmonertinib (INN pending; previously known as furmonertinib) is an oral, highly brain penetrant, broadly active, selective, epidermal growth factor receptor (EGFR) inhibitor engineered for broad activity and selectivity across EGFR mutations (mts)[a].
- Firmonertinib has been granted U.S. FDA Breakthrough Therapy Designation for the treatment of patients with previously untreated, locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) with EGFR exon 20 insertion (ex20ins) mts.
- EGFR ex20ins mutations occur in approximately 2% of NSCLC and overall account for approximately 9% of all the EGFR mts in NSCLC[b]. Current first-line (1L) standard of care (SOC) for NSCLC patients with this mutation is platinum-based chemotherapy[c].
- Additional presentations on pre-clinical data for firmonertinib activity in the uncommon EGFR mts **(Abstract 1964, Poster Session Section 25, Monday Apr 8th, 9:00AM- 12:30PM**) and a Phase Ib evaluating firmonertinib in activating EGFR or HER2 mts (**FURTHER, FURMO-002, Poster Section 50, Monday Apr 8 1:30 PM – 5:00 PM, CT152**) will be presented at AACR 2024 (see Resources and Contact).
- In the ongoing phase 1b study (FAVOUR study), firmonertinib showed promising efficacy in both treatment naïve and previously treated patients with NSCLC harboring EGFR ex20ins mts.
  - In treatment naïve (first-line treatment) patients, the confirmed Objective Response Rate (ORR) was 78.6% with a preliminary median Duration of Response (DoR) of 15.2 months (Table 1).
  - Responses were consistent across near-loop, far-loop and helical ex20ins mutations (Figure 1).
  - Firmonertinib showed a well-tolerated safety profile with the most observed treatment-related adverse event (TRAE) at 240mg dose being low-grade diarrhea[d].

| Table 1. Efficacy by IRC | Treatment Naïve 240mg N=28 | Previously Treated 240mg N= 26 | Previously Treated 160mg N= 26 |
|---|---|---|---|
| **Confirmed ORR, % (95% CI)** | 78.6% (59.0%, 91.7%) | 46.2% (26.6%, 66.6%) | 38.5% (20.2%, 59.4%) |
| **DoR, median (months) (95% CI)** | 15.2 (8.7, 24.8) | 13.1 (5.6, 13.8) | 9.7 (5.6, NA) |
| **Disease Control Rate (DCR) (CR+PR+SD) (95% CI)** | 100.0% (87.7%, 100.0%) | 92.3% (74.9%, 99.1%) | 84.6% (65.1%, 95.6%) |

Analysis is based on EGFR exon 20ins patients who had measurable disease at baseline by Independent Review Charter (IRC), had ≥ 2 tumor assessments, had progression of disease (PD)/death, or discontinued from treatment.

Figure 1. Depth of Response by Cohort and EGFR ex20ins Mutation Type




Waterfall plot was based on patients with at least one tumor assessment post baseline;
Near-loop region: A767-P772; far-loop region: H773-C775; Helical region: E762-M766

## FURVENT Trial Design

Figure 2: Patients with previously untreated, locally advanced or metastatic NSCLC with EGFR ex20ins mutations (N = 375)

→ Randomized 1:1:1

- Firmonertinib 240 mg QD
- Firmonertinib 160 mg QD
- Platinum + Pemetrexed Chemotherapy

## Trial Design

- A global study to investigate the efficacy and safety of firmonertinib compared to platinum-based chemotherapy as first-line treatment for patients with locally advanced or metastatic NSCLC with EGFR ex20ins mutations (Figure 2).
- Enrollment of 375 patients is planned and randomized 1:1:1 to receive firmonertinib 160 mg, firmonertinib 240 mg, or platinum-based chemotherapy (cisplatin or carboplatin plus pemetrexed for 4 cycles followed by pemetrexed maintenance therapy).
- Patients from the platinum-based chemotherapy arm with disease progression following chemotherapy are eligible to participate in the crossover phase to firmonertinib therapy.

## Key Endpoints

**Primary Endpoint**

- The primary endpoint is progression-free survival (PFS) comparing the treatment arms (firmonertinib 160 mg or 240 mg vs chemotherapy) based on blinded independent central review (BICR) assessment by RECIST v1.1

**Secondary Endpoints**

- Overall survival (OS), Investigator assessed PFS, Objective response rate (ORR), Duration of response (DOR)
- CNS-ORR, CNS DOR, CNS PFS

| Key Inclusion Criteria | Key Exclusion Criteria |
|---|---|
| Locally advanced or metastatic non-squamous NSCLC not amenable to curative surgery or radiotherapy | Severe acute or chronic infections |
| Documented EGFR ex20ins mutation detected in tumor tissue or blood from local or central testing | Previous interstitial lung disease (ILD) including drug-induced ILD or active ILD/radiation pneumonitis |
| Patients with a history of treated CNS metastases or new asymptomatic CNS metastases may be eligible | Mean resting QTcF > 470 msec |
| Patients with 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 chronic diarrhea, short bowel syndrome or significant upper GI surgery including gastric resection, a history of inflammatory bowel disease, or any active bowel inflammation |
| No prior systemic anticancer therapy for locally advanced or metastatic NSCLC including prior treatment with any EGFR TKIs | History of other malignancy within 3 years prior to screening, with the exception of patients with a negligible risk of metastases or death and/or treated with expected curative outcome |

## Statistical Methods

- The primary efficacy is PFS comparing the 2 treatment arms with the control chemotherapy arm.
- A stratified log-rank test will be performed for the primary comparison of PFS.
- OS will be analyzed similarly to the PFS endpoint.

## Accrual

- Global enrollment in this study is ongoing.

## Resources and Contact

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|---|---|
| FURVENT: NCT05607550<br>www.clinicaltrials.gov/study/NCT05607550 | |
| Firmonertinib (Furmonertinib) is a brain-penetrant EGFR TKI highly active in uncommon EGFR mutations, including PACC and exon 20 insertions (**Abstract 1964, Poster Session Section 25, Monday Apr 8th, 9:00AM- 12:30PM**) | |
| FURTHER: NCT05364043<br>www.clinicaltrials.gov/ct2/show/NCT05364073 | |
| For any additional questions:<br>furmo@arrivent.com | |

## References

a) Musib L, Kowanetz M, Li Q, Luo H, Hu J, Lutzker S. Pp01. 11 furmonertinib is an oral, irreversible, highly brain-penetrant pan-egfr inhibitor with activity against classical and atypical egfr mutations. Journal of Thoracic Oncology. 2023;18(3):e14-e15.
b) Robichaux JP, Le X, Vijayan RSK, et al. Structure-based classification predicts drug response in EGFR-mutant NSCLC. Nature. 2021;597(7878):732-737.
c) Ettinger DS, Wood DE, Aisner DL, et al. Non-small cell lung cancer, version 3. 2022, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2022;20(5):497-530.
d) Han et al, FAVOUR: A phase 1b study of furmonertinib, an oral, brain penetrant, selective EGFR inhibitor, in patients with advanced NSCLC with EGFR Exon 20 insertions. WCLC 2023.

## Acknowledgement

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