FURTHER (FURMO-002): Global Study to Evaluate Firmonertinib (Furmonertinib) in Patients with EGFR Mutant NSCLC Including Uncommon EGFR Mutations

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Background

- Firmonertinib (INN pending; also 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[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 mutations.
- Firmonertinib is approved in China for first-line advanced NSCLC with EGFR Ex19del or L858R mutations based on PFS benefit observed in the Phase 3 study versus gefitinib (FURLONG), and for previously treated, advanced NSCLC with EGFR T790M mutation.
- Uncommon EGFR mutations occur in approximately 30% of patients with EGFR-mutated NSCLC[b] including EGFR exon 20 insertion mutations as well as P-loop and αC-helix Compressing (PACC) mutations. PACC mutations are similar to exon 20 mutations in narrowing the drug-binding pocket. The most frequent EGFR PACC mutations include G719X, S768I, E709X, L747X, E709_T710delinsD, V769X and V774M.
- 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 mutations[c].
  - 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.
  - Firmonertinib showed a well-tolerated safety profile with the most observed treatment-related adverse event (TRAE) at 240mg dose being low-grade diarrhea.
- A Phase III study (FURVENT, FURMO-004) in first-line metastatic EGFR exon 20 insertion NSCLC Trials-in-Progress presentation is being presented at the AACR 2024 Annual Meeting [**Abstract CT280, Poster Session Section 50, Tuesday Apr 9th, 1:30PM – 5:00PM**] (see Resources and Contact).
- Firmonertinib is a potential therapeutic option for NSCLC patients with EGFR PACC mutations, based on pre-clinical in vitro and in vivo data [**Abstract 1964, Poster Session Section 25, Monday Apr 8th, 9:00AM- 12:30PM**] (see Resources and Contact).

Trial Design

- A global study to investigate the efficacy and safety of firmonertinib in patients with NSCLC with EGFR mutations or HER2 mutations.
- Enrollment of approximately 27 to 50 patients in Stage 1 (dose escalation and backfill cohorts) and approximately 120 patients across 4 expansion cohorts in Stage 2, receiving firmonertinib 240 mg QD or 160 mg QD.

DCR – disease control rate; PFS – progression-free survival; OS – overall survival

Key Endpoints

Stage 1 Primary Endpoint

Incidence and severity of adverse events (AEs), including DLTs, with severity determined according to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0)

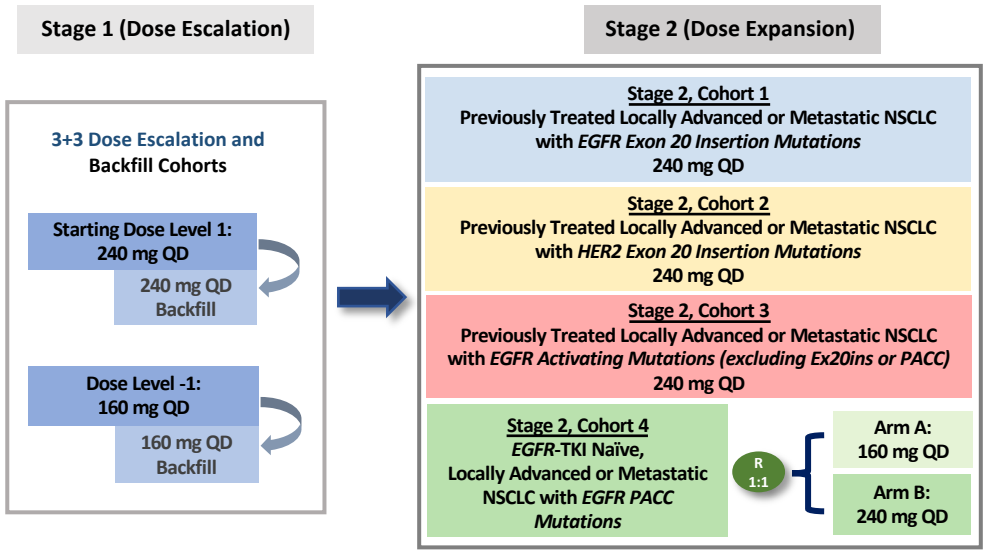
Stage 2 Primary Endpoint

- Confirmed objective response rate (ORR) by RECIST v1.1

Stage 2 Key Secondary Endpoint

- DoR, DCR, PFS, OS per RECIST v1.1

FURTHER Study Design



Key Inclusion Criteria

Locally advanced or metastatic NSCLC not amenable to curative surgery or radiotherapy.
Disease that has progressed after at least one available standard therapy; or for whom standard therapy has proven ineffective; or for whom a clinical trial of an investigational agent is recognized as standard of care.
Documented radiologic disease progression during or after the last systemic anti-cancer therapy before the first dose of firmonertinib.
Documented validated results from local testing of either tumor tissue or blood confirming presence of EGFR mutations or EGFR Uncommon mutations.
Stage 2 Cohort 4: Previously untreated in the locally advanced or metastatic setting or have progressed after at least 1 available standard therapy

Key Exclusion Criteria

Severe acute or chronic infections
Previous interstitial lung disease (ILD) including drug-induced ILD or active ILD/radiation pneumonitis. Mean resting QTcF > 470 msec
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
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
Stage 2 Cohort 4: Prior treatment with any EGFR TKIs. Progression during neoadjuvant or adjuvant therapy or within 12 months of completion of chemotherapy, radiotherapy, or immunotherapy.

Statistical Methods

- Stage 1: The number and percentage of patients with DLTs in the DLT window will be summarized by the dose levels in the dose-escalation stage for patients who are evaluable for DLT.
- Stage 2: The efficacy endpoints of confirmed ORR and DOR will be summarized by stage, cohort, indication, and/or dose as appropriate.

Accrual

- Global enrollment in this study is ongoing.

Resources and Contact

FURTHER: NCT05364043
www.clinicaltrials.gov/ct2/show/NCT05364073

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)

FURVENT: NCT05607550
www.clinicaltrials.gov/study/NCT05607550

For any additional questions:
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References

a) Musib L, Kowanetz M, Li Q, Luo H, Hu J, Lutzker S. Pp01. 11 firmonertinib 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) Han et al, FAVOUR: A phase 1b study of firmonertinib, an oral, brain penetrant, selective EGFR inhibitor, in patients with advanced NSCLC with EGFR Exon 20 insertions. WCLC 2023.

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