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

Alexander Spirai1, Byoung Chul Cho2, Enriqueta Felip1, Edward B. Garon3, Koichi Goto4, Melissa Johnson5, Natasha Leigh6, Antonio Passaro7, David Planchard8, Sanjay Popat9, James Yang10, Xiaojian Lu11, Yong Jiang12, Jack Huang13, Morgan Lam13, Marcin Kowanetz13, Shirley Wang13, John Le13, Jerry Y. Hsu13, Cai-Cun Zhou14

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.
- Firmonertinib has been granted U.S. FDA Breakthrough Therapy Designation for the treatment of patients with previously untreated, locally advanced or metastatic non-small 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. Current first-line (1L) standard of care (SOC) for NSCLC patients with this mutation is platinum-based chemotherapy.
- Additional presentations on preclinical data for firmonertinib activity in the uncommon EGFR mts (Abstract 1974, Poster Session Section 24, Monday Apr 8th, 9:00AM-12:30PM) and a finding of evaluating firmonertinib in activating EGFR or HER2 mts (FURTHER, FURMOCO-002, Poster Session 50, Monday Apr 8 1:30 PM – 5:00 PM, CT012) will be presented at AACR 2023 (see Resources and Contact).

In the ongoing phase 1b study (FAVOUR study), firmonertinib showed promising efficacy in both treatment naive and previously treated patients with NSCLC harboring EGFR ex20ins mts.
- In treatment naive (1L) 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 diarrhoea.

Key Inclusion Criteria:
- Locally advanced or metastatic non-squamous NSCLC not amenable to curative surgery or radiotherapy
- Documented EGFR ex20ins mutation detected in tumor tissue or blood from local or central testing
- Patients with a history of treated CNS metastases or new asymptomatic CNS metastases may be eligible

Key Exclusion Criteria:
- Severe acute or chronic infections
- Previous interstitial lung disease (ILD) including drug-induced ILD
- Significant upper GI surgery including gastric resection, a history of treated CNS metastases or new asymptomatic CNS metastases
- Mean resting QTcF > 470 msec
- Previous interstitial lung disease (ILD) including drug-induced ILD
- Severe acute or chronic infections
- Patients with a history of treated CNS metastases or new asymptomatic CNS metastases may be eligible

FURVENT 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).
- Enrolment 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 (BIR) as assessed by RECIST v1.1.
- Secondary Endpoints:
  - Overall survival (OS), Investigator assessed PFS, Objective response rate (ORR), Duration of response (DOR), Severe adverse events (SAEs) in all treatment arms.
  - CNS-ORR, CNS DOR, CNS PFS

Analysis of firmonertinib ex20ins patients who had measured disease at baseline by Independent Review (IRC), had 2 tumor assessments, had progression of disease (PD), or discontinued treatment.

Table 1. Efficacy by IRC

<table>
<thead>
<tr>
<th>Treatment Naive 240mg</th>
<th>Treatment Previously Untreated 240mg</th>
<th>Treatment Previously Treated 160mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed ORR, % (95% CI)</td>
<td>78.8% (59.0%, 91.7%)</td>
<td>62.9% (42.6%, 80.8%)</td>
</tr>
<tr>
<td>DoR, median (months) (95% CI)</td>
<td>15.2 (8.7, 24.8)</td>
<td>13.1 (6.6, 13.8)</td>
</tr>
<tr>
<td>Disease Control Rate (DCR) (ORR+SD+PD)</td>
<td>100.0% (87.7%, 100.0%)</td>
<td>92.3% (74.9%, 99.1%)</td>
</tr>
</tbody>
</table>

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

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

Statistical Methods
- The primary endpoint 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.

Acknowledgement
- We thank the patients, their families/caregivers, and investigators and site staff teams who are making this trial possible.
- FURVENT study is funded by ArriveBioPharma, Inc. and Shanghai Alsil Pharmaceuticals Inc.

References

Resources and Contact
- Furmonertinib is a brain-penetrant EGFR T-R0 highly active in uncommon EGFR mts, including PACC and exon 20 insertions (Abstract 1974, Poster Session Section 24, Monday Apr 8th, 9:00AM-12:30PM).
- FURTHER: NCT05364043

For any additional questions: furmo@arrivent.com