BMC Cancer

RESEARCH

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EGFR exon 20 insertions mutation in lung adenocarcinoma and its response by high-dose of Furmonertinib: a real-world study

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Abstract

Background LUAD patients with EGFR exon 20 insertions (ex20ins) have a poorer prognosis than those with EGFR 19del or L858R mutations. The FAVOUR study showed high-dose furmonertinib's efficacy in ex20ins patients. However, more real-world data are needed to validate these findings.

Methods We summarized LUAD patients who underwent NGS testing at Henan Cancer Hospital from January 1, 2020, to December 31, 2022. We then reviewed cases of patients with EGFR exon 20 insertion (ex20ins) mutations who received high-dose furmonertinib (240 mg/day) and had follow-up data. We assessed the objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), time to treatment failure (TTF), overall survival (OS), and treatment-related adverse events (TRAEs).

Results A total of 3,571 patients underwent NGS testing, with 1,632 (45.70%) identified as having EGFR mutations, including 87 (2.44%) with exon 20 insertions (ex20ins). Follow-up data were complete for 21 ex20ins patients treated with 240 mg/d of furmonertinib. Thirteen had prior treatments, including targeted therapy, and four had received EGFR-TKI. By March 1, 2024, 18 patients progressed, and 13 died. The ORR was 52.40% (11/21), DCR was 100%, median PFS was 6.15 months, TTF was 10.78 months, and OS was 21.67 months. Among the 18 progressing patients, 11 had neurological progression, six had thoracic progression, and two had liver progression. Diarrhea was the most common adverse event, and no patients discontinued treatment due to AEs.

Conclusions Among LUAD patients, 2.44% harbored EGFR exon 20 insertions (ex20ins), and furmonertinib at 240 mg/d demonstrated efficacy and was well-tolerated in this real-world study of LUAD patients with EGFR ex20ins mutations.

Keywords EGFR, Furmonertinib, Lung adenocarcinoma, EGFR ex20ins

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Background

Lung cancer is one of the most common malignancies in humans, with the highest cancer-related mortality worldwide [1]. Non-small cell lung cancer (NSCLC), accounting for approximately 90% of all lung cancer cases, is the most prevalent histological type. Lung adenocarcinoma and lung squamous cell carcinoma are the major subtypes of NSCLC. Lung adenocarcinoma (LUAD) patients often harbor driver gene mutations and can be effectively treated with targeted therapies [2]. The most common driver gene mutation in lung adenocarcinoma is EGFR, with frequent mutations such as exon 19 deletions (19del) and exon 21 L858R, which can be managed with EGFR-targeted tyrosine kinase inhibitors (EGFR-TKIs) [3]. Rare mutations like S768I and L861Q can be treated with afatinib [4]. However, EGFR exon 20 insertion mutations (EGFR ex20ins), occurring in about 10% of EGFR-mutated NSCLC cases, are less responsive to approved EGFR-TKIs [5, 6]. These mutations alter the spatial structure of the drug-binding pocket, creating steric hindrance that prevents traditional first- to third-generation EGFR TKIs from binding effectively [7]. Consequently, patients with EGFR ex20ins have a poorer prognosis and derive limited benefit from EGFR-TKI treatment.

Furmonertinib is a novel third-generation EGFR-TKI featuring a trifluoroethoxy structure while retaining the core structure of third-generation EGFR-TKIs. This functional group confers strong hydrophobicity, high lipid solubility, and significant electron-withdrawing properties [8]. These characteristics provide furmonertinib with unique molecular and pharmacological advantages. Both Furmonertinib (AST2818) and its metabolite (AST5902) effectively inhibit EGFR ex20ins mutations while having minimal inhibitory effects on wild-type EGFR [9, 10].

In dose-escalation (NCT02973763) and dose-expansion (NCT03127449) studies, patients received furmonertinib at doses of 20 mg, 40 mg, 80 mg, 160 mg, or 240 mg once daily [18]. In the dose-expansion phase (40–240 mg), the overall objective response rate (ORR) was 76.70% (89 of 116), including 70.60% (12 of 17) in patients with central nervous system metastases. Treatment-related adverse events (AEs) occurred in 79% of patients (103 of 130), with 8% experiencing grade 3 or higher AEs (11 of 130). Serious AEs were reported in 15% of patients (20 of 130), with two cases related to treatment. Notably, no significant increase in adverse effects was observed at the 240 mg QD dose [11].

The FAVOUR study (a Phase 1b trial) demonstrated the efficacy and tolerability of furmonertinib at 160 mg/d and 240 mg/d in EGFR ex20ins patients [11]. Given furmonertinib's potential to inhibit EGFR mutations and its favorable safety profile at higher doses, we hypothesize that increasing the dose of targeted drugs could improve outcomes for patients with EGFR ex20ins. Therefore, we treated advanced LUAD patients with EGFR ex20ins who refused chemotherapy with a triple dose (240 mg QD) of furmonertinib starting January 1, 2021.

Methods

Participants

We summarized LUAD patients who underwent NGS testing at Henan Cancer Hospital from January 1, 2020, to December 31, 2022. Patients with advanced LUAD harboring EGFR exon 20 insertion (ex20ins) mutations, either untreated or progressed after prior treatment, with an ECOG performance status of 0–2, and who refused chemotherapy, were included in the study. All patients were from Henan Cancer Hospital and had follow-up data from January 1, 2021, to March 1, 2024.

We treated 21 advanced LUAD patients harboring EGFR ex20ins mutations who declined chemotherapy with a triple dose (240 mg QD) of furmonertinib. The higher dose was chosen based on the findings of the FAVOUR study and the rationale that escalating the dose of targeted therapies may enhance clinical outcomes for patients with EGFR ex20ins [11, 12].

Clinicopathological characteristics, including gender, age, smoking history, histological type, EGFR mutation status at diagnosis, and gene mutation status before treatment, were collected from medical records. Pre-treatment physical condition was assessed using the ECOG Performance Status (ECOG-PS). Treatment information included previous EGFR-TKI use, other systemic and local treatments such as chemotherapy, surgery, and radiotherapy, as well as the type and grade of adverse events during furmonertinib 240 mg/d treatment. The initiation date of furmonertinib treatment, time to tumor progression, and patient death dates were also recorded. All patients provided informed consent, and the study received ethics committee approval.

Assessment of efficacy and safety

This retrospective, single-center, real-world study aimed to assess the efficacy and safety of furmonertinib 240 mg/day in patients with EGFR exon 20 insertion (ex20ins) mutations. The clinical data collected and analyzed included progression-free survival (PFS), overall survival (OS), objective response rate (ORR), disease control rate (DCR), time to treatment failure (TTF), and safety and tolerability. Oncologic efficacy was evaluated according to RECIST version 1.1.

Progression-free survival (PFS) was defined as the time from the initiation of 240 mg/day furmonertinib to disease progression or death from any cause, whichever occurred first. Overall survival (OS) was defined as the time from the start of treatment to death from any cause. Objective response rate (ORR) was defined as the proportion of patients achieving complete response

(CR) or partial response (PR), based on a ≥ 20% reduction in tumor diameter maintained for at least 4 weeks. Disease control rate (DCR) was defined as the proportion of patients achieving CR, PR, or stable disease (SD). Time to treatment failure (TTF) was defined as the time from the start of furmonertinib treatment to discontinuation due to lack of benefit. As of the end of the follow-up, among the 21 patients, 3 still showed no progression and 8 remained alive. Patients were censored at the last follow-up date if they were alive or had not experienced progression or death at that time.

Safety and tolerability were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0. Control of central nervous system (CNS)-related symptoms was based on patient-reported outcomes.

Statistical analysis

Survival curves were estimated using the Kaplan-Meier method, and differences between groups were compared using the log-rank test. A two-sided p-value < 0.05 was considered statistically significant.

Results

Molecular characterization of EGFR Ex20ins mutations

From January 1, 2020, to December 31, 2022, a total of 3,571 patients underwent NGS testing at Henan Cancer Hospital. Among them, 1,632 (45.70%) had EGFR mutations, with 87 (2.44%) harboring ex20ins mutations. Including patients who were tested in other hospitals and subsequently treated at our hospital, the total number of patients with EGFR ex20ins was 94. Of these, 87 patients were identified with specific subtypes by NGS, while seven were detected by PCR.

A total of 38 specific variants were identified (Table 1). The most common insertional mutation was p.A767_V769dup (28.74%), followed by p.S768_D770dup (12.64%), p.N771_P772insH (4.60%), and p.A763_Y764insFQEA (4.60%). Consistent with previous studies [5], the majority of insertion sites (80 out of 87) were located in the P-loop, while the remaining seven were in the C-helix.

Clinical characteristics of EGFR Ex20ins mutations

As of the follow-up date from January 1, 2021, to March 1, 2024, a total of 21 LUAD patients with EGFR ex20ins mutations were included in the study, of whom 13 had died. The clinical characteristics of these 21 patients are summarized in Table 2. The patients' ages ranged from 33 to 80 years, with 12 patients younger than 55 and 9 patients aged 55 or older. The cohort included 12 females and 9 males. Smoking history was noted for 4 patients, while 17 were non-smokers. Thirteen patients had received prior treatments, including targeted therapy; among these, 7 had received TKI treatment, with 4 specifically receiving EGFR-TKI therapy. Ten patients had CNS metastasis, while 11 did not.

Efficacy of 240 mg/d Furmonertinib in advanced LUAD with EGFR ex20ins

As of the follow-up date from January 1, 2021, to March 1, 2024, among the 21 patients with advanced LUAD harboring EGFR ex20ins mutations who received 240 mg/d furmonertinib, 20 had evaluable lesions (Fig. 1). After treatment with 240 mg/d furmonertinib, 10 patients achieved PR, and 1 patient CR, resulting in an ORR of 52.40%. Lesions were stable in 9 patients, while in another case, the disease was stable but the lesion was not measurable. The DCR was 100%. Of the 21 patients, 18 have progressed: neurological progression in 11/18, thoracic progression in 6/18, liver progression in 2/18, and other sites in 1/18. (Supplementary Table 1)

As of the follow-up date from January 1, 2021, to March 1, 2024, 18 out of 21 patients have progressed, and 17 out of 21 have discontinued furmonertinib treatment. Thirteen out of 21 patients have died. The median PFS for the 21 patients was 6.15 months, the median time to TTF was 10.78 months, and the median OS was 21.67 months (Fig. 2).

Table 1 Molecular characterization of the 87 EGFR ex20ins mutations

Subtypes	Number of each subtype	Mutation frequency of each subtype
p.A767_V769dup	25	28.74%
p.S768_D770dup	11	12.64%
p.N771_P772insH; p.A763_Y764insFQEA	4	4.60%
p.A767_S768insSVD; p.D770_N771insG; p.D770_N771insSVD; p.H773dup; p.N771delinsKT; p.M766_A767insASV; p.P772_H773insHA; p.772_H773insTNP; p.S768_V769delinsIL;	2	2.30%
p.N771_P772delinsGGT; p.D770_N771insY; p.D770_P772dup; p.D770delinsGNPH; p.D770delinsGY; p.H773_V774delinsLM; p.H773_V774dup; p.N771_H773dup; p.N771_P772insG; p.N771_P772insT; p.N771_P772insV; p.N771delinsKH; p.N771delinsRH; p.N771dup; p.P772_H773dup; p.P772_H773insGNNP; p.P772_H773insGNP; p.P772_H773insHT; p.S768_V769insVAS; p.V769_D770insASV; p.V769_D770insG; p.V769_D770insGSV; p.V769_D770insGTR; p.V769_D770insSSV; p.M766delinsMASV	1	1.15%

Table 2 Clinical characteristics of the 21 LUAD patients with EGFR 20ins mutation

Characteristics	Frequency	Deaths (%)
Total	21	13 (61.90)
Age		
≤55	12	7 (58.33)
>55	9	6 (66.67)
Sex		
Male	9	7 (77.78)
Female	12	6 (50.00)
Smoking status		
Never	17	9 (52.94)
Former	4	4 (100.00)
Prior treatment		
Yes	13	11 (84.62)
No	8	2 (25.00)
Prior TKI treatment		
Yes	7	5 (71.43)
No	14	8 (57.14)
CNS metastasis		
Yes	10	8 (80.00)
No	11	5 (45.45)

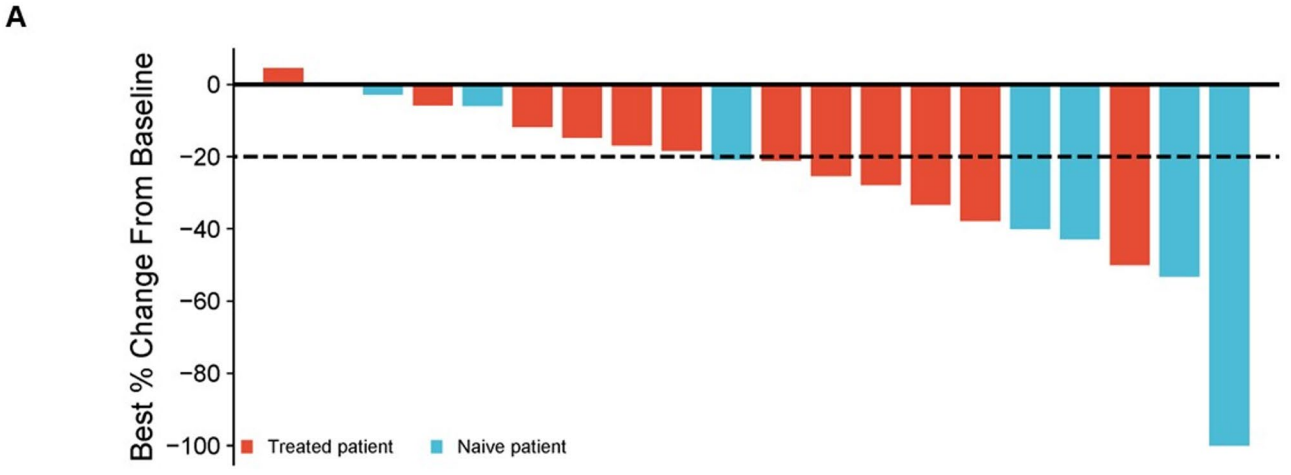

Fig. 1 As of the follow-up date from January 1, 2021, to March 1, 2024, after treatment with 240 mg/d furmonertinib, 10 patients achieved PR and 1 patient achieved CR. The ORR was 52.4% (11/21). Lesions were stable in 9 patients, and in one case, the disease was stable but the lesion was not measurable. DCR: 100% (21/21)

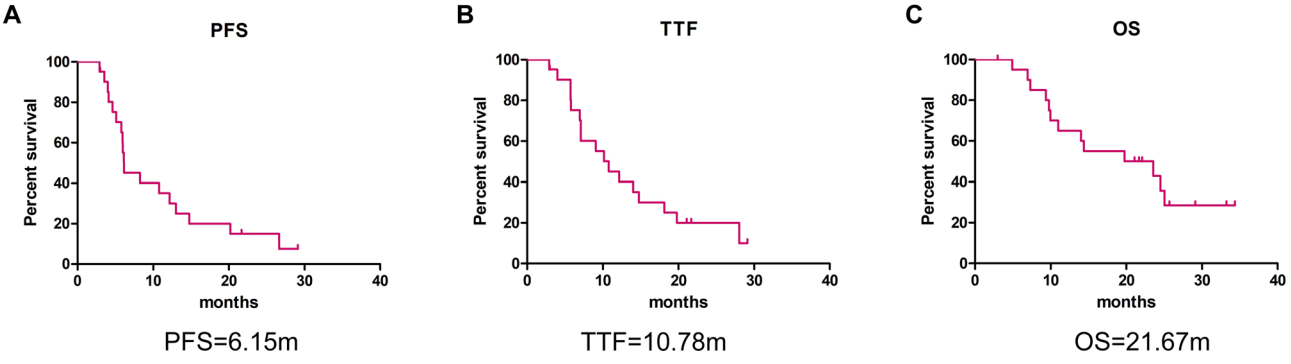

Fig. 2 In 21 patients with advanced LUAD harboring EGFR ex20ins mutations treated with 240 mg/d furmonertinib, the median PFS was 6.15 months (**A**), the median TTF was 10.78 months (**B**), and the median OS was 21.67 months (**C**) as of the follow-up date from January 1, 2021, to March 1, 2024

The patients were classified into two groups according to whether they had undergone systemic treatment previously. Of the 21 patients, 13 had prior treatments, and 8 were treatment-naïve. Among the 8 treatment-naïve patients, 5 (62.50%) achieved PR or CR after receiving 240 mg furmonertinib, compared to 6 out of 13 (46.15%) previously treated patients (Fig. 1). There was a significant difference between untreated and treated patients in PFS, TTF, and OS. The PFS in treatment-naïve patients was significantly longer at 21.19 months compared to 5.79 months in previously treated patients (HR 0.19, 95% CI 0.07–0.54, $p = 0.002$) (Fig. 3A). The TTF in treatment-naïve patients was 28.04 months compared to 7.1 months in previously treated patients (HR 0.15, 95% CI 0.05–0.44, $p < 0.001$) (Fig. 3B). The OS in treatment-naïve patients was not reached, compared to 11.01 months in previously treated patients (HR 0.28, 95% CI 0.09–0.84, $p = 0.023$) (Fig. 3C).

Central nervous system (CNS) metastasis is a challenging issue in lung cancer treatment. The patients were classified into two groups in accordance with the presence or absence of central nervous system metastasis. Among the 21 patients, 10 had CNS metastasis, and 11 did not. Although no statistically significant differences were observed, patients without CNS metastasis showed a trend toward extended PFS, TTF, and OS. The PFS in patients without CNS metastasis was 6.12 months compared to 6.15 months in those with CNS metastasis (HR 0.49, 95% CI 0.18–1.36, $p = 0.169$) (Fig. 3D). The TTF in patients without CNS metastasis was 14.01 months compared to 9.07 months in those with CNS metastasis (HR 0.41, 95% CI 0.15–1.17, $p = 0.097$) (Fig. 3E). The OS in patients without CNS metastasis was not reached, compared to 19.76 months in those with CNS metastasis (HR 0.57, 95% CI 0.19–1.70, $p = 0.312$) (Fig. 3F).

Standard doses of EGFR-TKIs are often insufficient to effectively inhibit EGFR ex20ins mutations. Increasing the therapeutic dose of third-generation EGFR-TKIs has emerged as a potentially effective strategy. One patient in our study was previously treated with 165 mg almonertinib (standard dose 110 mg QD) from September 24, 2021, achieving stable disease (SD) for five months. However, due to adverse reactions, the almonertinib dose could not be further increased. Subsequently, the patient switched to 240 mg/d furmonertinib (triple the standard dose of 80 mg QD) and achieved PR after two months of treatment. This case demonstrates that increasing the dose of third-generation EGFR-TKIs can achieve efficacy, but adverse reactions may limit dose escalation. Furmonertinib's advantage lies in its low incidence of adverse reactions, allowing for effective treatment of EGFR ex20ins mutations under tolerable conditions by increasing the dose to 240 mg/d (Fig. 4).

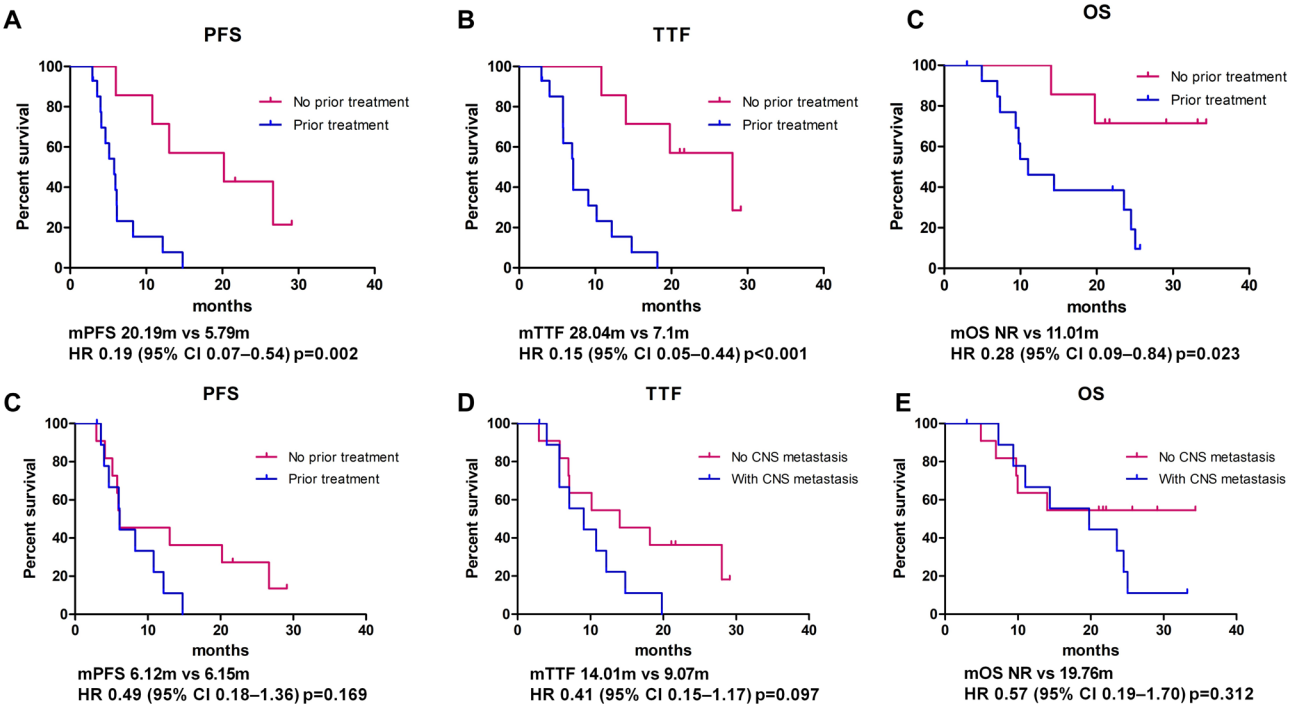

Fig. 3 As of the follow-up date from January 1, 2021, to March 1, 2024, among the 21 patients with advanced LUAD harboring EGFR ex20ins mutations, 13 had received prior systemic therapy, while 8 had not. Compared with patients who received prior systemic therapy, those who did not had significantly longer PFS (**A**), TTF (**B**), and OS (**C**). Of the 21 patients, 10 had central nervous system (CNS) metastasis, and 11 did not. Patients without CNS metastasis tended to have prolonged PFS (**D**), TTF (**E**), and OS (**F**) compared to those with CNS metastasis

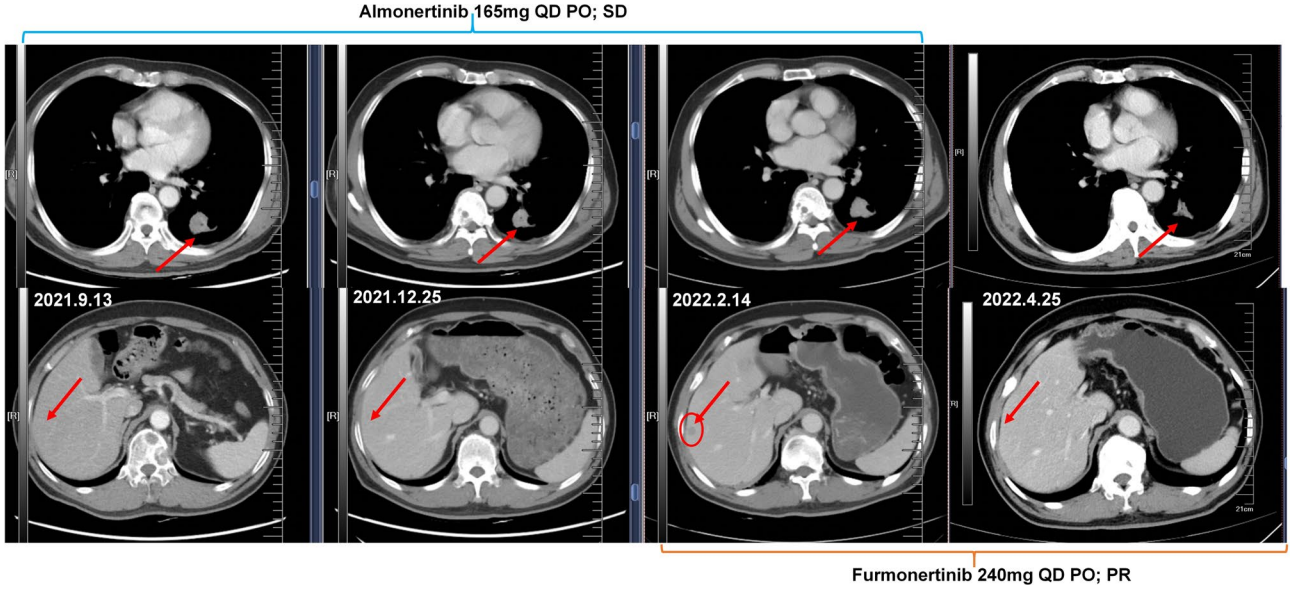

Fig. 4 A patient diagnosed with LUAD harboring an EGFR exon 20 insertion mutation on September 17, 2021, began treatment with almonertinib (a third-generation EGFR-TKI with a standard dose of 110 mg QD) at 165 mg QD from September 24, 2021. The curative effect was evaluated as SD until February 14, 2022, when progressive PD was confirmed. Subsequently, the patient switched to 240 mg/d furmonertinib (standard dose 80 mg QD) and achieved PR after two months of treatment

Table 3 TRAEs of 240 mg Furmonertinib in the 21 LUAD patients with EGFR ex20ins mutation

TRAEs	(of Patient %)	AEs (TRAEs) ≥10%	All grade	Grade 3 or higher
All TRAE	20 (95.2%)	Diarrhea	16 (76.19%)	2(9.52%)
Grade 3 or higher	2 (9.52%)	Anemia	8 (38.10%)	0
SAE	1 (4.76%)	AST Increased	5 (23.81%)	0
TRAE leading to death	0	ALT Increased	5 (23.81%)	0
TRAE leading to dose interruption	0	Creatinine Increased	3 (14.29%)	0
TRAE leading to dose reduction	1 (4.76%)	Dental ulcer	7 (33.33%)	0
TRAE leading to discontinuation	0	Rash	9 (42.86%)	0
		ECG QT prolongation	5 (23.81%)	0
		WBC Decreased	6 (28.57%)	0
		Loss of appetite	3 (14.29%)	0
		Paronychia	5 (23.81%)	0

Safety

As of the follow-up date from January 1, 2021, to March 1, 2024, treatment-related adverse events (TRAEs) were recorded for the 21 LUAD patients with EGFR ex20ins mutations who received 240 mg furmonertinib. As shown in Table 3, TRAEs occurred in 20 out of 21 (95.24%) patients. Grade 3 or higher TRAEs were observed in 2 out of 21 (9.52%) patients. One patient (4.76%) experienced a serious adverse event (SAE) of diarrhea. One patient (4.76%) had a TRAE leading to dose reduction, and no TRAEs resulted in dose interruption.

Discussion

EGFR ex20ins mutations present a unique challenge in the treatment of NSCLC [13]. Unlike common EGFR mutations such as exon 19 deletions or L858R in exon 21, ex20ins mutations are associated with resistance to conventional EGFR-targeted therapies like gefitinib and erlotinib, as well as newer generation TKIs such as osimertinib [14, 15]. Chemotherapy-based regimens have limited efficacy in first-line treatment for patients with EGFR ex20ins mutations [16, 17].

Research in this area aims to develop effective targeted therapies specifically tailored to patients with EGFR ex20ins mutations. Structural biology techniques have been employed to better understand the unique conformational changes caused by ex20ins in the EGFR protein, guiding the design of more potent and selective inhibitors [18]. The crystal structure of the EGFR ex20ins mutant NPG subtype overlaps significantly with that of wild-type EGFR, especially at the osimertinib binding site, making it challenging to develop new drugs with both efficacy and safety [15]. Combination therapies have also been explored to enhance the efficacy of targeted treatments

[19], including combinations with other targeted agents, immunotherapy, or chemotherapy [5, 20].

Targeted therapies specifically designed for EGFR ex20ins mutations in NSCLC are still under development, and few drugs are specifically indicated for this mutation [20]. However, several investigational agents have shown promising results in clinical trials. Mobocertinib (TAK-788), an oral EGFR TKI designed to target tumors with EGFR ex20ins, demonstrated antitumor activity in a phase 1/2 study (EXCLAIM), with an ORR of around 28% and a DCR of approximately 78% [21]. In September 2021, the FDA granted accelerated approval to mobocertinib for treating EGFR ex20ins NSCLC after platinum-containing chemotherapy failure. However, due to the failure of the EXCLAIM-2 Phase 3 study, Takeda voluntarily withdrew mobocertinib from the U.S. market in October 2023 [22].

Poziotinib is an irreversible pan-Her TKI with activity against EGFR, HER2, and HER4, making it a potential option for patients with EGFR ex20ins mutations [23]. Clinical studies, including phase 2 trials, have shown promising activity of poziotinib in patients with NSCLC harboring EGFR ex20ins, with ORRs ranging from 27 to 64%. However, gastrointestinal side effects, particularly diarrhea, have been notable adverse events associated with poziotinib [24].

Amivantamab (JNJ-61186372) is a bispecific antibody targeting EGFR and MET, which has shown activity in NSCLC patients with EGFR ex20ins mutations [25]. In a phase 1 study (CHRYSALIS), amivantamab demonstrated promising efficacy with an ORR of approximately 40% in heavily pretreated patients with EGFR exon 20 insertion mutations [26]. Positive results from the PAPILLON Phase 3 study were published, showing that the median progression-free survival (PFS) assessed by blinded independent central review (BICR) was 11.4 months (95% CI: 9.8–13.7) in the combination chemotherapy group compared to 6.7 months (95% CI: 5.6–7.3) in the chemotherapy group, with a significantly longer PFS in the combination group (HR, 0.40). The 18-month PFS rate was 31% in the amivantamab plus chemotherapy group versus 3% in the chemotherapy group. The ORR was 73% (95% CI: 65–80) with a median duration of response (DOR) of 9.7 months (95% CI: 8.2–13.5) in the amivantamab plus chemotherapy group. In the chemotherapy group, the ORR was 47% (95% CI: 39–56) with a median DOR of 4.4 months (95% CI: 4.1–5.6) [27].

Sunvozertinib is an oral, potent, irreversible inhibitor, highly selective for multiple EGFR mutant subtypes, including EGFR ex20ins mutations [28]. The WU-KONG6 phase 2 study in China showed best-in-class efficacy for sunvozertinib in platinum-based treated NSCLC patients with EGFR ex20ins mutations. Tumor responses were achieved in 59 out of 97 patients, with an ORR of 61% (95% CI: 50%, 71%), reaching statistical significance ($p < 0.001$). The DCR was 88% (95% CI: 79%, 93%). Subgroup analysis showed that sunvozertinib had antitumor efficacy across different mutation subtypes and insertion locations, with ORRs exceeding 50% [29].

Positive results were also obtained in the FAVOUR Phase 1b study of furmonertinib in EGFR ex20ins mutation patients. A total of 86 patients were included. Independent review committee (IRC) results showed confirmed ORRs of 78.6%, 46.2%, and 38.5% for the initial 240 mg, treated 240 mg, and treated 160 mg groups, respectively. Median DOR were 15.2 months, 13.1 months, and 9.7 months, respectively. In October 2023, the FDA granted breakthrough therapy designation to furmonertinib for the treatment of primary EGFR ex20ins NSCLC [12].

Our study is the first to explore the real-world treatment of LUAD patients with EGFR ex20ins mutations using 240 mg/d furmonertinib and achieve OS results. The results showed that in the real world, the ORR reached 52.40%, DCR reached 100%, PFS reached 6.15 months, and initial treatment patients could reach 20.19 months. OS reached 21.67 months, and initial treatment patients could exceed 30 months. Furmonertinib's advantage is its relatively low incidence of adverse reactions, enabling effective treatment of EGFR ex20ins mutations under tolerable conditions through dose escalation to 240 mg/day. Among the 21 patients, only 2 experienced Grade 3 TRAEs, and no TRAEs led to dose interruption. The most common site of progression was brain metastases, and the most common adverse event was diarrhea, with only one patient reducing the dose to 160 mg due to an adverse event.

Increasing the dose intensity of drugs is a common strategy for resolving tumor drug resistance. However, for the majority of drugs, their relatively significant adverse reactions have restricted further escalation of the dose intensity, such as osimertinib and almonertinib. Based on the previous dose escalation study, 240 mg (three times the normal dose) constitutes the maximum tolerated dose of furmonertinib [11]. Hence, a dose of 240 mg was administered to the patient for treatment. In this study, one patient progressed after treatment with almonertinib at 165 mg/day, but still responded effectively to treatment with furmonertinib at 240 mg/day. This indicates that enhancing the dose intensity can effectively treat EGFR ex20ins when the adverse reactions are tolerable.

Limitation

This was a single-center retrospective study with only 21 patients and no control group for 160 mg and 80 mg doses. As of the end of the follow-up, among the 21 patients, 3 still showed no progression and 8 remained alive. These patients were regarded as censored data

in the statistical analysis. The data come from the real world, and the evidence level of the research results is not high, but they can supplement previous similar studies. Larger sample size studies and dose comparison groups are needed to validate the research results and optimize the dosing regimen.

Conclusion

LUAD patients had a 2.44% incidence of EGFR ex20ins mutations. Furmonertinib is a promising targeted therapy for EGFR ex20ins mutations. At 240 mg/d, furmonertinib was effective and well-tolerated. Further data from ongoing clinical trials will be crucial in determining its efficacy and safety profile in the treatment landscape for this challenging subtype of NSCLC.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-14313-7.

Supplementary Material 1

Author contributions

S. Y. and Y. L. wrote the main manuscript text. J. Z. and Z. H. followed up and collected information about the patients. H. C., S. M. and Yufeng. W. prepared Figs. 1 and 2. Yingxi. W. and L. W. prepared Figs. 3 and 4. C. Z. prepared all tables. Q. W. propose and design the topic. All authors reviewed the manuscript.

Funding

This work was supported by a project cosponsored by Key Research and Development Projects of Henan Province in 2023 - Key technologies of novel precision immunotherapy for refractory malignant tumors (No. 231111313300); Henan Province Health and Youth Subject Leader Training Project (No. [2020]60); Key project of medical science and technology in Henan Province (SBGJ202101009); Leading Talent Cultivation Project of Henan Health Science and Technology Innovation Talents (YXKC2020009); ZHONGYUAN QIANREN JIHUA (ZYQR201912118); Wu Jie-ping Clinical Research Fund (320.6750.2021-02-121) and The Excellent Young Talent Cultivation Project of Henan Health Science and Technology Innovation Talents (No. YXKC2022050). It was also supported by Henan International Joint Laboratory of drug resistance and reversal of targeted therapy for lung cancer (No. [2021]10); Henan Refractory Lung Cancer Drug Treatment Engineering Technology Research Center (No. [2020]4); and Henan Medical Key Laboratory of Refractory lung cancer (No. [2020]27). The funders had no role in the study design, data collection, analysis, decision to publish, or manuscript preparation.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study has been approved by the Ethics Committee of the Affiliated Cancer Hospital of Zhengzhou University (2022-247-003), adhering to Helsinki Declaration, with informed consent waived due to its retrospective nature.

Consent for publication

This manuscript has not been published or presented elsewhere in part or in entirety, and is not under consideration by another journal. All the authors have approved the manuscript and agree with submission to your esteemed journal.

Competing interests

The authors declare no competing interests.

Received: 8 January 2025 / Accepted: 12 May 2025
Published online: 20 May 2025

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