

P3.223: Firmonertinib (160mg) Combined with Chemotherapy as First-Line Treatment for Advanced NSCLC Patients with EGFR Mutations and CNS Metastases

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Background

- Central nervous system (CNS) metastases are common in EGFR-mutated NSCLC and are associated with poor prognosis¹.
- Firmonertinib is an oral, highly CNS-penetrant, third-generation EGFR tyrosine kinase inhibitor (TKI), which has been approved for the first-line treatment of patients with 19Del or L858R mutations and treatment of patients with T790M mutations whose disease has progressed on or after EGFR TKI therapy²⁻³.
- Previous study has demonstrated that CNS efficacy of firmonertinib 160mg is superior to firmonertinib 80mg⁴.
- This study aimed to evaluate the efficacy and safety of firmonertinib (160mg) combined with pemetrexed and platinum-based chemotherapy as a first-line treatment for non-small cell lung cancer (NSCLC) patients with EGFR mutations and CNS metastases.

METHODS

- This prospective, single-arm, phase II clinical study enrolled untreated NSCLC patients with EGFR classic mutations and CNS metastases from multiple medical centers in Anhui Province between January 30, 2024 and January 8, 2026.
- A total of 25 participants have been fully enrolled and are still ongoing with follow-up.
- All patients received a combination therapy of firmonertinib (160mg), pemetrexed plus platinum-based chemotherapy. Clinical baseline characteristics, efficacy outcomes, and safety data were systematically collected and analyzed.

Patients

- Of the 25 eligible patients, 11 (44%) were male and the median age was 65 years, 25 (100%) had ECOG scores of 1, 19 (76%) had multiple CNS metastatic sites.
- Among the 25 patients, 13 (52%) had EGFR exon 19 deletions, and 12 (48%) had L858R mutations, with 7 (28%) also presenting TP53 co-mutations.

Table 1. Baseline characteristics of patients

Characteristics	Patients, N (%) N=25
Age (years) Median (range)	65 (34, 76)
Sex , Male/Female	11 (44%) / 14 (56%)
ECOG PS , 0/1	0 (0%) / 25 (100%)
Smoking history , Yes/No/Unknown	3 (12%) / 21 (84%) / 1 (4%)
CNS metastatic site , Single/Multiple	6 (24%) / 19 (76%)
EGFR mutation , 19Del/858R	13 (52%) / 12 (48%)
TP53 mutation	7 (28%)

Efficacy

- At data cutoff (March, 2026), the objective response rate (ORR) and CNS ORR were 88% and 84%, while the disease control rate (DCR) and CNS DCR were 100% and 96%, respectively.
- With a median follow-up of 6.7 months, 21 patients are still on study treatment, with only 4 patients of disease progression from the study. Progression-free survival (PFS) and CNS PFS data were not yet mature.

RESULTS

Table 2. Systemic and CNS treatment response

N(%)	Systemic tumor response (N=25)	CNS response (N=25)
CR	0	8 (32%)
PR	22 (88%)	13 (52%)
SD	3 (12%)	3 (12%)
PD	0	0
Not evaluabe	0	1 (4%)
ORR, %	88%	84%
DCR, %	100%	96%

Table 3. Overview of TRAEs

AEs (# of Patient, %)	N=25
Total TEAE	23 (92%)
≥3 grade TEAE	9 (36%)
Total TRAE	23 (92%)
≥3 grade TRAE	8 (32%)
Treatment related SAE	0
TRAE related deaths	0
TRAE related discontinuations	2 (8%)
TRAE related dose reductions	3 (12%)
TRAE related dose interruptions	4 (16%)

Safety

- The safety profile of the combination therapy was manageable.
- Treatment-related adverse events (TRAEs) of grade ≥3 occurred in 32% of patients, with the most common adverse events were anemia and leukopenia, which were more strongly associated with chemotherapy.
- However, no grade 4 adverse events or treatment-related deaths were reported.

CONCLUSION

- Firmonertinib (160mg) combined with pemetrexed and platinum-based chemotherapy demonstrated promising clinical efficacy and manageable toxicity in EGFR-mutated NSCLC patients with CNS metastases. These findings support its potential as a viable first-line treatment option for this patient population.

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