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Stereotactic radiotherapy(SRT) in combination with Aumolertinib to treat intracranial oligometastatic Non-Small Cell Lung Cancer (NSCLC): An update of the phase II, prospective study

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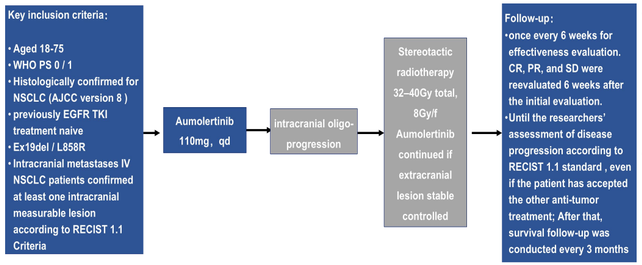
Background

- Aumolertinib is a tolerable third-generation epidermal growth factor receptor tyrosine kinase inhibitor that has CNS efficacy in patients with EGFR-mutant NSCLC.
- Stereotactic radiotherapy (SRT) is highly effective and less toxic for limited intracranial metastases.
- We aim to investigate the efficacy and safety of aumolertinib followed by SRT in patients with intracranial oligometastatic NSCLC.

Methods

- Intracranial oligometastatic Patients with EGFR sensitive mutations(EGFR-TKIs naive) were enrolled and received aumolertinib 110mg daily until intracranial disease progression.
- Then SRT (32–40Gy total, 8Gy/f) was given to intracranial oligo-progression disease if possible.
- The primary endpoint was intracranial objective response rate (iORR). Secondary endpoints included intracranial progression-free survival (iPFS), intracranial duration of response (iDOR)according to RECIST 1.1, cerebral radiation necrosis rate (CRNR) and overall survival (OS).
- Safety was evaluated according to Common Terminology Criteria for Adverse Events version 5.0 (CTCAE v5.0).
- This trial is registered with ClinicalTrials.gov, NCT04519983.



Results

Patients

- To January 6, 2023, a total of 35 patients were enrolled and 32 patients were assessible followed for 3 months to 16 months.
- All patients received 110mg aumolertinib daily and received at least one independent imaging evaluation by a radiologist.

Table 1. Patient demographic characteristics

Characteristics	N=35
Age, mean (range), years	60(36-81)
Gender: male/female, %	15/20
Adenocarcinoma, %	100%
Smoking status-ever/never, %	12/23
ECOG score: 0/1, %	22/13
EGFR mutation: Ex19del/L858R, %	19/16

Efficacy

- After oral administration of aumolertinib, the best response of all patients in intracranial and extracranial lesions was partial response (PR), with an intracranial objective response rate of 100%.
- At data cut-off, one patient developed intracranial primary lesion progression at 12 months after oral administration of aumolertinib but stable in extracranial lesions. SRT treatment was given to this patient.

Table 2. Summary of Confirmed CNS Response

CNS Response	N = 32
CNS ORR*, % (95% CI)	100%
Complete response (CR), No. (%)	3
Partial response（PR）, No. (%)	29
Not evaluable, No. (%)	0
CNS DCR, % (95% CI)	100%

Safety

- No grade ≥3 adverse events occurred after continued oral administration of aumolertinib.
- The most common adverse reactions were rash and abnormal liver enzymes, 1 patient had grade 2 CK elevation.

Table 3. Most Frequent Safety Events

Commonly reported AEs (≥ 20%, all causality), n (%)	N = 32	
	Any Gr	CTCAE ≥ Gr 3
Any AEs		
Alanine aminotransferase increased	2	0
Aspartate aminotransferase increased	2	0
Rash	5	0
White blood cell count decresed	1	0
Platelet count decrease	1	0
Blood creatine phosphokinase increased	1	0
Constipation	1	0

Conclusions

- This report showed pronounced intracranial objective response benefit in patients with intracranial oligometastatic disease followed by SRT after intracranial oligo-progression and no new safety signals.
- Aumolertinib has promising efficacy and good tolerability in intracranial oligometastatic EGFR mutated NSCLC.

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