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A phase IIa study to evaluate safety and efficacy of Rezivertinib (BPI-7711) in locally advanced or metastatic/recurrent treatment-naïve NSCLC patients with EGFR mutation

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BACKGROUND

- **Rezivertinib (BPI-7711)** is a novel third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) targeting both EGFR-sensitizing mutations and EGFR T790M mutation. In a previous phase I study, rezivertinib resulted in an objective response rate (ORR) of 59.3%, a disease control rate (DCR) of 91.3%, and a median progression-free survival (PFS) of 9.7 months for advanced non-small cell lung cancer (NSCLC) patients with EGFR T790M mutation, and the recommended phase II dose (RP2D) was identified as 180 mg once daily.
- This study aimed to evaluate the efficacy and safety of rezivertinib in locally advanced or metastatic/recurrent **treatment-naïve NSCLC patients with EGFR-sensitizing mutation.**

OBJECTIVE

- The primary endpoint was objective response rate (ORR) assessed by blinded independent central review (BICR) per the Response Evaluation Criteria In Solid Tumours version 1.1 (RECIST v1.1). The efficacy for patients with central nervous system (CNS) metastases was measured by BICR according to the Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM).
- Secondary endpoints included disease control rate (DCR), duration of response (DoR), progression-free survival (PFS), overall survival (OS) and safety. Safety was assessed as per the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.

METHODS

- This was a multicenter, single-arm, open-label, phase IIa study **(NCT03386955)** conducted across 20 sites in the People's Republic of China.
- **Treatment-naïve** NSCLC patients with locally advanced or metastatic/recurrent EGFR-sensitizing mutation received 180mg rezivertinib once daily until unacceptable toxicity, disease progression, or withdrawal of consent.
- Treatment beyond progression was permitted if clinical benefits could be obtained in the judgement of the investigators.

BASELINE CHARACTERISTICS

- From Jun 12, 2019, to Oct 17, 2019, 43 **treatment-naïve**, **EGFR-sensitizing mutated** advanced NSCLC patients were enrolled;
- **12(27.9%)** patients had CNS metastases;
- By the data cut-off date on Dec 23, 2021, the median duration of follow-up was **25.3 (95% CI: 25.0-26.2)** months.

Figure 1. The Study Design and Procedures of Rezivertinib (BPI-7711) phase IIa study

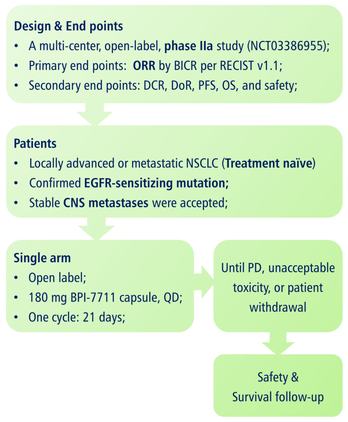


Table 1. Baseline Characteristics

Characteristics	Overall, n (%)
Age Group, n (%)	
< 50 years	6 (14.0)
50 - 65 years	20 (46.5)
≥ 65 years	17 (39.5)
Sex, n (%)	
Female	23 (53.5)
Male	20 (46.5)
Race, n (%)	
Asian (Chinese)	43 (100.0)
ECOG PS	
0	6 (14.0)
1	37 (86.0)
EGFR mutation type	
Exon 19 deletion	28 (65.1)
L858R	13 (30.2)
Other	2 (4.7)
CNS metastases	
Yes	12 (27.9)
No	31 (72.1)

Note: EGFR, epidermal growth factor receptor; CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; PS, performance status;

EFFICACY

- The tumor shrinkage was observed in 95.3% (41/43) of patients; The ORR was 83.7% (95% CI: 69.3-93.2) by BICR and DCR was 97.7% (95% CI: 87.7-99.9);
- The median DoR was 19.3 (95% CI: 15.8-25.0) months by BICR; **The median PFS was 22.0 (95% CI: 16.8-26.3) months by investigators and 20.7 (95% CI: 13.8-24.8) months by BICR.**
- For all patients with CNS metastases, the CNS-ORR was 50.0% (95% CI: 21.1-78.9) and CNS-DCR was 58.3% (95% CI: 27.7-84.8); The 12-month CNS progression-free rate was 66.7%;
- For patients with baseline brain target lesion, the CNS-ORR was 80.0% (28.4-99.5) and CNS-DCR was 100.0% (47.7-100.0).

Figure 2. Waterfall plot for best percentage change from baseline by BICR in FAS

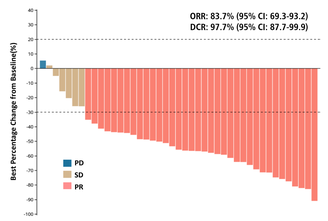
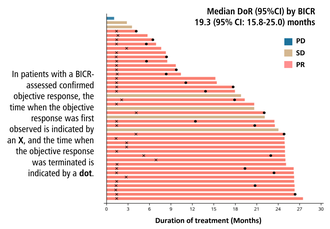


Figure 3. Swimmer plot for duration of treatment.



Note for Figure 2 and Figure 3: BICR, blinded independent center review; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate; CI, confidence interval; FAS, full analysis set;

Table 2. Efficacy of Rezivertinib in FAS

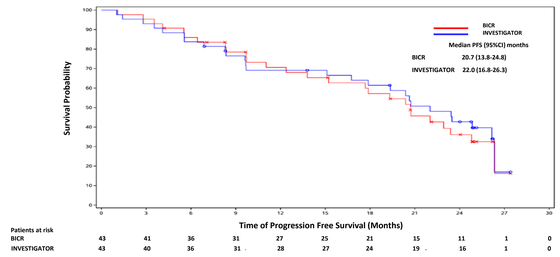
	BICR-assessed (n=43)	Investigator-assessed (n=43)
Overall response, n (%)		
Complete response	0	0
Partial response	36 (83.7)	30 (69.8)
Stable disease	6 (14.0)	11 (25.6)
Progressive disease	1 (2.3)	2 (4.7)
ORR, n (%)	36 (83.7)	30 (69.8)
95% CI, %	69.3 to 93.2	53.8 to 83.0
DCR, n (%)	42 (97.7)	41 (95.3)
95% CI, %	87.7 to 99.9	84.2 to 99.4
Median DoR, months	19.3	19.3
95% CI	15.8 to 25.0	8.3 to 25.0
Median PFS, months	20.7	22
95% CI	13.8 to 24.8	16.8 to 26.3

Table 3. CNS Efficacy of Rezivertinib by BICR in FAS

	Brain Metastasis in FAS (n=12)	Patients with Baseline Brain Target Lesion (n=5)
CNS response, n (%)		
Complete response	2 (16.7)	0
Partial response	4 (33.3)	4 (80.0)
Stable disease	1 (8.3)	1 (20.0)
Non-CR/Non-PD	5 (41.7)	0
Progressive disease	0	0
CNS ORR, n (%)	6 (50.0)	4 (80.0)
95% CI, %	21.1-78.9	28.4-99.5
CNS DCR, n (%)	7 (58.3)	5 (100.0)
95% CI, %	27.7-84.8	47.7-100.0
12-month CNS progression-free rate, %	66.7	60.0

Note of Table 2 and Table 3: BICR, blinded independent center review; ORR, objective response rate; DCR, disease control rate; CI, confidence interval; DoR, Duration of response; PFS, progression-free survival; CNS, central nervous system; FAS, full analysis set;

Figure 4. Kaplan-Meier plot for progression-free survival (PFS) by BICR and investigator in FAS



Note: BICR, blinded independent center review; CI, confidence interval; FAS, full analysis set;

SAFETY

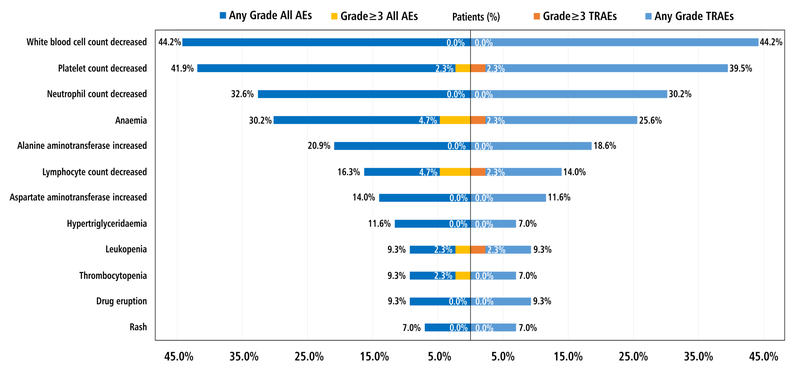
- All 43 patients were included in the safety set; 40 (93.0%) patients had treatment related adverse events (TRAEs) while 4 (9.3%) had grade 3 TRAEs; **No grade ≥4 TRAEs or treatment-related serious events were reported;**
- The top three TRAEs were white blood cell count decreased (44.2%), platelet count decreased (39.5%), neutrophil count decreased (30.2%);
- **No interstitial lung disease was reported.**

Table 4. Safety Summary of Rezivertinib

AE Category	Total, n (%) (n=43)
Any AE	42 (97.7)
Grade≥3 AE	16 (37.2)
TRAE	40 (93.0)
Grade≥3 TRAE	4 (9.3)
Dose interruption due to AE	3 (7.0)
Dose reduction due to AE	0
Discontinuation due to AE	3 (7.0)
Discontinuation due to TRAE	0
Any serious event	12 (27.9)
Treatment-related serious event *	0

Note: AE, adverse event, TRAE, treatment related adverse event; *As assessed by investigator.

Figure 5. The most common (Incidence>5%) TRAEs of Rezivertinib in safety set



CONCLUSIONS

Rezivertinib showed promising efficacy and favorable safety for locally advanced or metastatic/recurrent NSCLC patients with EGFR-sensitizing mutation at first-line setting:

- The tumor shrinkage was observed in 95.3% (41/43) of patients, with an ORR of 83.7% by BICR, the median PFS of 22.0 months by investigators, and 20.7 months by BICR, respectively ;
- Rezivertinib also showed promising efficacy for patients who had CNS metastases, with the CNS-ORR of 50.0% and CNS-DCR of 58.3%; for patients with baseline brain target lesion, the CNS-ORR was 80.0% and CNS-DCR was 100.0% ;
- Rezivertinib revealed a favorable and manageable safety profile after over 2 years follow-up as well.

DISCLOSURE OF COMPETING INTERESTS

- M. Greco, T. Wang and F. Mo are the employees of Beta Pharma, and all other authors declare no competing interests.

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