Updated Efficacy and Safety of Pralsetinib in Chinese Patients with Advanced RET Fusion+ Non-Small Cell Lung Cancer

Q. Zhou[1], Y.-L. Wu[1], J. Zhao[2], J. Chang[3], H. Wang[3], Y. Fan[4], K. Wang[5], G. Wu[6], W. Nian[7], Y. Gong[7], Y. Sun[8], M. Sun[8], X. Wang[9], H. Shi[9], X. Zheng[10], M. Qin[11], X. Duan[11], Z. Shen[11], S. Yao[11], J. Yang[11]

[1] Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China; [2] Beijing Cancer Hospital, Beijing, China; [3] Fudan University Shanghai Cancer Center, Shanghai, China; [4] Zhejiang Cancer Hospital, Hangzhou, China; [5] West China Hospital Sichuan University, Chengdu, China; [6] Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [7] Chongqing Cancer Hospital, Chongqing, China; [8] Jinan Central Hospital, Jinan, China; [9] First Affiliated Hospital of Gannan Medical University, Ganzhou, China; [10] Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; [11] CStone Pharmaceuticals (Suzhou) Co., Ltd., Suzhou, China;

SINGAPORE 2022 ESMO ASIA

389P

BACKGROUND

- Rearranged during transfection (RET) fusions were reported as oncogenic drivers in 1.4 to 2.3% of Chinese non-small cell lung cancer (NSCLC) patients[1-2].
- Pralsetinib (formerly BLU-667) is a highly potent and selective kinase inhibitor designed to specifically target RET fusions and mutations. ARROW, a global phase I/II study (NCT03037385) has demonstrated durable antitumor activity of pralsetinib in advanced RET-altered solid tumors[3]. This led to the approvals of pralsetinib by the U.S. FDA for the treatment of metastatic RET fusion+ NSCLC, advanced RET fusion+ thyroid cancer and RET-mutant medullary thyroid cancer, and by the EMA for the treatment of advanced RET fusion+ NSCLC not previously treated with a RET inhibitor.
- Pralsetinib has also shown consistent results in the Chinese patients and is the first selective RET inhibitor approved by China NMPA in two indications - locally advanced or metastatic, RET fusion+, platinum-treated NSCLC (March 2021), and advanced RET-mutant MTC and RET fusion+ thyroid cancer (March 2022).
- Here, with a longer follow-up, we present the updated efficacy and safety data of pralsetinib in Chinese patients with advanced RET fusion+ NSCLC from two phase II cohorts in ARROW study.

METHODS

Key inclusion/exclusion criteria and endpoints:

- **Inclusion:** aged ≥18 years with non-resectable locally advanced or metastatic NSCLC; Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1; having documented RET fusion per local testing. **Exclusion:** having central nervous system(CNS) metastases associated with progressive neurological symptoms or requiring increasing doses of corticosteroids to control the CNS disease were excluded; patients with other known driver alteration.
- Primary endpoints were overall response rate (ORR) by blinded independent central review (BICR) per RECIST v1.1 and safety profile. Key secondary endpoints were duration of response (DOR), clinical benefit rate (CBR), disease control rate (DCR), progression-free survival (PFS) and overall survival (OS).

Treatment:

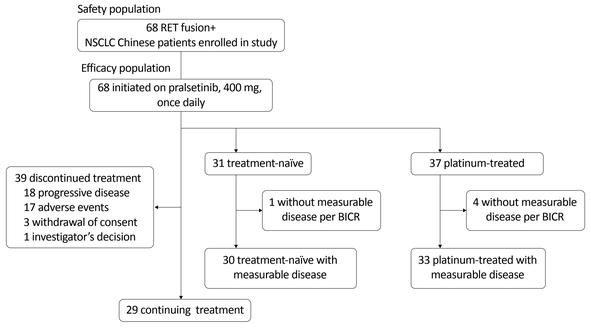
- Pralsetinib at 400 mg once daily orally (as established RP2D in Phase I).

Assessment:

- Tumor assessment was assessed per RECIST v1.1 by BICR.
- Adverse events (AEs) were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Event (NCI-CTCAE) V4.03.

RESULTS

Figure 1. Patients Disposition in Chinese NSCLC Cohorts



- As of 4 March 2022, 68 Chinese patients with RET fusion+ NSCLC had received pralsetinib 400 mg (safety and efficacy population), of whom 31 were treatment-naïve and 37 were platinum-treated **(Figure 1)**.
- At the data cut-off, the median duration of follow-up was 17.8 months in treatment-naïve patients and 27.2 months in platinum-treated patients.

Baseline Characteristics

Table 1. Baseline Characteristics in Chinese NSCLC Cohorts (Safety Population)

Characteristic	Treatment-Naïve (n=31)	Platinum-Treated (n=37)
Age, years, median (range)	57 (30,79)	54 (26,77)
<65 years, n (%)	22 (71.0)	29 (78.4)
Sex, male, n (%)	11 (35.5)	17 (45.9)
ECOG performance status, n (%)		
0	1 (3.2)	2 (5.4)
1	30 (96.8)	35 (94.6)
Histology type, n (%)		
Adenocarcinoma	31 (100)	36 (97.3)
Other	0	1 (2.7)
CNS metastasis, n (%)	8 (25.8)	15 (40.5)
TNM stage at screening , n (%)		
Stage IIIB/ IIIC	2 (6.5)	0
Stage IVA	12 (38.7)	8 (21.6)
Stage IVB	17 (54.8)	29 (78.4)
Prior anticancer regimens, n (%)		
Median (range)	0	2.0 (1–9)
1	0	14 (37.8)
2	0	5 (13.5)
3	0	6 (16.2)
>3	0	12 (32.4)
Prior systemic therapy type, n (%)		
Platinum-based chemotherapy	0	37 (100.0)
Multikinase inhibitors	0	14 (37.8)
PD-1/PD-L1 inhibitors	0	14 (37.8)
Smoking history, n (%)		
Never smoked	21 (67.7)	25 (67.6)
Former/Current	10 (32.3)	12 (32.4)
RET-Fusion Partner, n (%)		
KIF5B	22 (71.0)	23 (62.2)
CCDC6	5 (16.1)	7 (18.9)
Other	4 (12.9)	7 (18.9)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; CNS, Central Nervous System; TNM, Tumor Node Metastasis; PD-1/PD-L1, Programmed Cell Death-1/Programmed Cell Death-Ligand 1; RET, Rearranged during Transfection.

Efficacy

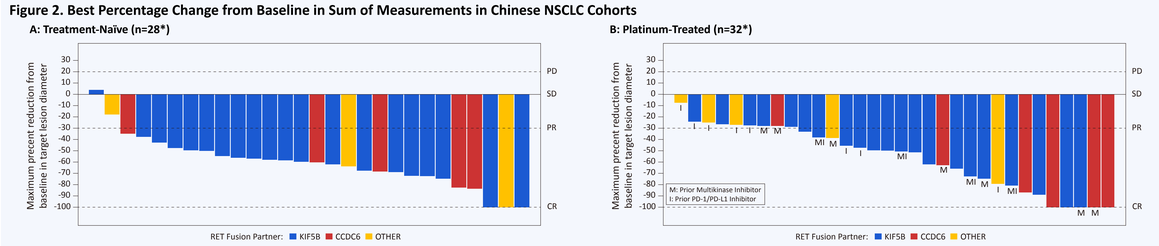
- Confirmed ORR in treatment-naïve and platinum-treated patients were 83.3% (95% CI: 65.3-94.4) and 66.7% (95% CI: 48.2-82.0) respectively.

Table 2. Efficacy Summary in Chinese NSCLC Cohorts (Efficacy Population with measurable disease at baseline)

Outcome	Treatment-Naïve (n=30)	Platinum-Treated (n=33)
Confirmed ORR, n(%) [95% CI]	25 (83.3) [65.3-94.4]	22 (66.7) [48.2-82.0]
CR, n(%)	2 (6.7)	1 (3.0)
PR, n(%)	23 (76.7)	21 (63.6)
SD, n(%)	1 (3.3)	9 (27.3)
PD, n(%)	2 (6.7)	1 (3.0)
NE, n(%)	2 (6.7)	1 (3.0)
CBR*, % (95% CI)	86.7 (69.3-96.2)	84.8 (68.1-94.9)
DCR, % (95% CI)	86.7 (69.3-96.2)	93.9 (79.8-99.3)

Abbreviations: ORR, Objective Response Rate; CR, Complete Response; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease; NE, Not evaluable; CBR, Clinical Benefit Rate; DCR, Disease Control Rate.
*Confirmed CR, PR or SD>=16 weeks

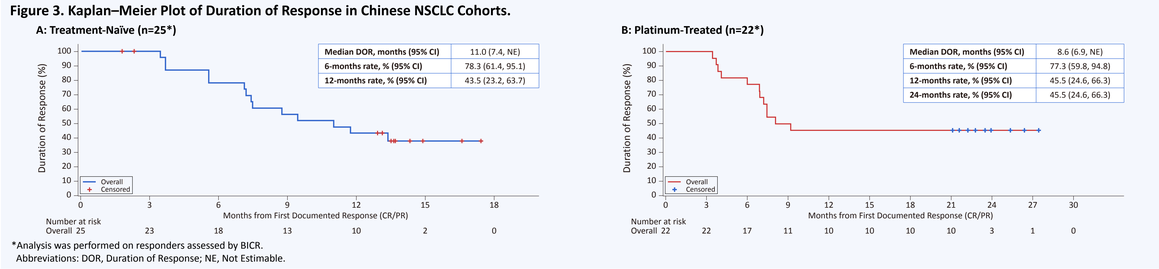
Figure 2. Best Percentage Change from Baseline in Sum of Measurements in Chinese NSCLC Cohorts



*2 treatment-naïve patients and 1 platinum-treated patient were not included due to absence of evaluable post-baseline disease response assessment by BICR per RECIST v1.1

- The median DOR in treatment-naïve and platinum-treated patients were 11.0 months (95% CI: 7.4, NE) and 8.6 months (95% CI: 6.9, NE) respectively.

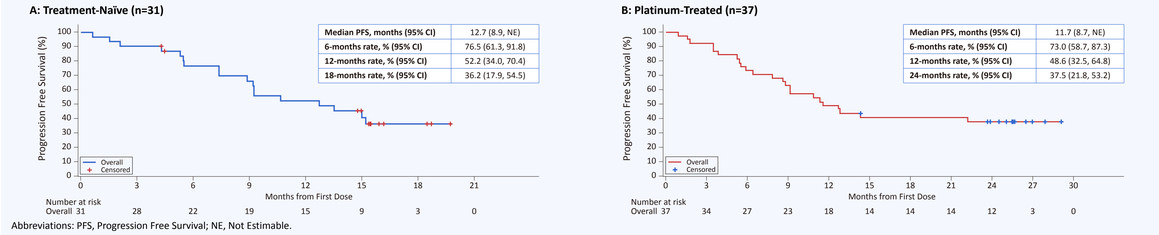
Figure 3. Kaplan–Meier Plot of Duration of Response in Chinese NSCLC Cohorts.



*Analysis was performed on responders assessed by BICR.
Abbreviations: DOR, Duration of Response; NE, Not Estimable.

- The median PFS was 12.7 months (95% CI: 8.9, NE) in treatment-naïve patients and 11.7 months (95% CI: 8.7, NE) in platinum-treated patients.

Figure 4. Kaplan–Meier Plot of Progression Free Survival in Chinese NSCLC Cohorts (Efficacy Population)



Abbreviations: PFS, Progression Free Survival; NE, Not Estimable.

- The median OS in both treatment-naïve and platinum-treated patients had not been reached as of 4 March 2022.

Table 3. Summary of Treatment-Related Adverse Events (TRAEs) in Chinese NSCLC patients (N=68)

Patients with AE by PT	n (%)	
	Any grade	Grade ≥3
Aspartate aminotransferase increased	56 (82.4)	3 (4.4)
Neutrophil count decreased	54 (79.4)	23 (33.8)
Anaemia	49 (72.1)	24 (35.3)
White blood cell count decreased	42 (61.8)	9 (13.2)
Alanine aminotransferase increased	39 (57.4)	3 (4.4)
Blood creatine phosphokinase increased	31 (45.6)	13 (19.1)
Hypertension	25 (36.8)	10 (14.7)
Blood creatinine increased	22 (32.4)	1 (1.5)
Platelet count decreased	21 (30.9)	6 (8.8)
Bilirubin conjugated increased	20 (29.4)	0
Constipation	19 (27.9)	0
Gamma-glutamyltransferase increased	19 (27.9)	4 (5.9)
Blood alkaline phosphatase increased	18 (26.5)	2 (2.9)
Blood bilirubin increased	17 (25.0)	2 (2.9)
Malaise	17 (25.0)	0
Diarrhoea	15 (22.1)	2 (2.9)
Hypocalcaemia	15 (22.1)	1 (1.5)
Leukopenia	15 (22.1)	4 (5.9)

The table includes TRAEs which occurred in ≥20% of patients. Abbreviations: AE, Adverse Event; PT, Preferred Term.

Safety

- In the safety population (n=68), the median duration of treatment were 16.7 months for treatment-naïve patients and 19.5 months for platinum-treated patients.
- The most frequently reported AEs were hematological and serum chemistry laboratory abnormalities. Pralsetinib-related AEs were manageable with supportive care and dose modification.
- Overall, 11.8% of patients discontinued pralsetinib due to treatment-related adverse events (TRAEs).

CONCLUSIONS

- With longer follow-up, pralsetinib continues to demonstrate deep and durable response and long-term clinical benefit in RET fusion+ NSCLC Chinese patients with or without prior platinum treatment.
- Updated results are consistent with previously reported results from the global population in the ARROW trial. Pralsetinib in Chinese patients has a manageable safety profile, with no new safety signals detected.
- Overall, pralsetinib showed a favorable benefit-risk profile, offering a transformative medicine to Chinese RET-fusion driven advanced NSCLC patients.

DISCLOSURES

Qing Zhou (email address: gzzhouqing@126.com) reports lecture and presentations fees to herself from AstraZeneca, Boehringer Ingelheim, BMS, Eli Lilly, MSD, Pfizer, Roche, and Sanofi.

ACKNOWLEDGEMENTS

This study was sponsored by CStone Pharmaceuticals (Suzhou) Co., Ltd, Suzhou, China and Blueprint Medicines Corporation. We thank all the patients, their families, all investigators and site research staffs participated in this study. Medical writing assistance was provided by Yuanyuan Dai, of CStone Pharmaceuticals (Suzhou) Co., Ltd.

REFERENCES

1.Wen S, et al. Oncologist. 2019;24:e1070-e81; 2.Zhang K, et al. Oncol Res. 2019;27:575-82; 3.Gainor JF, et al. Lancet Oncol 2021;5:42–50.

Scan to download a reprint of this poster