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

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Introduction: 111
RET fusion has been identified as an oncogenic driver in approximately 1-2% of patients with NSCLC. Pralsetinib is a highly potent and selective inhibitor of RET and oncogenic RET alterations. ARROW is a phase I/II, open-label, and first-in-human study to evaluate the safety and antineoplastic activity of pralsetinib in a variety of advanced RET altered solid tumors including NSCLC. Previously we reported the efficacy and safety results of pralsetinib in a cohort of Chinese patients with RET fusion+ NSCLC after platinum-based chemotherapy at WCLC 2020. Here we present updated results of this cohort and also report the results of pralsetinib in a cohort of Chinese NSCLC patients without prior systemic treatment.

Methods: 72
RET fusion+ Chinese NSCLC patients without or with prior platinum-based chemotherapy were enrolled and administered with pralsetinib 400 mg QD. The primary endpoints are the objective response rate (ORR) by blinded independent central review per RECIST v1.1 and safety profile, assessed by incidence, severity, and type of AEs in Chinese patients. The secondary endpoints include duration of response (DOR), clinical benefit rate (CBR), disease control rate (DCR), progression-free survival, and overall survival.

Results: 135+100

As of 12 April 2021, 68 Chinese patients with RET fusion+ NSCLC (37 previously treated with platinum-based chemotherapies and 31 systemic treatment-naïve) received pralsetinib. At baseline, most (95.6%) patients had ECOG performance score of 1. The RET fusion partners (66.2% KIF5B, 17.6% CCDC6, 16.2% other) and the prevalence of brain metastases (33.8%) were similar to the global population. The efficacy results are shown in the table. Pralsetinib shows high ORRs in Chinese RET fusion+ NSCLC patients regardless of prior therapy. All patients treated with at least 1 dose of pralsetinib were included in the safety analysis (n=68). The most frequently reported treatment-related adverse events (TRAEs) included aspartate aminotransferase increased (80.9%), neutrophil count decreased (79.4%), anemia (67.6%), white blood cell count decreased (60.3%), and alanine aminotransferase increased (57.4%). 10.3% of patients discontinued pralsetinib due to TRAEs.

Outcome	**Prior platinum-based chemotherapy treatment (n=33) [a]**	**No prior systemic treatment (n=30) [a]**
ORR, % (95% CI)	66.7 (48.2 - 82.0)	80.0 (61.4 - 92.3)
CR, %	3.0	6.7
PR, %	63.6	73.3
SD, %	27.3	6.7
PD, %	3.0	6.7
NE, %	3.0	6.7
CBR, % (95% CI)	84.8 (68.1 - 94.9)	86.7 (69.3 - 96.2)
DCR, % (95% CI)	93.9 (79.8 - 99.3)	86.7 (69.3 - 96.2)
Responders' outcome	**Prior platinum-based chemotherapy treatment (n=22)**	**No prior systemic treatment (n=24)**
Median time to first response (CR/PR), months (min, max)	1.89 (1.7 - 5.6)	1.87 (1.7 - 3.8)
6-month DOR rate, % (95% CI)	77.3 (59.8 - 94.8)	76.7 (55.6 - 97.8)
9-month DOR rate, % (95% CI)	50.0 (29.1 - 70.9)	38.3 (0.0 - 92.5)

[a] Efficacy population with measurable disease at baseline.
CR=complete response; PR=partial response; SD=stable disease; PD=progressive disease; NE=not evaluable.

Conclusions: 81

Pralsetinib is a promising targeted therapy with rapid and deep clinical activity in RET fusion+ NSCLC Chinese patients regardless of prior therapies. Efficacy results are consistent with previously reported data from the global population in the ARROW trial, and in treatment naïve Chinese patients pralsetinib shows the same efficacy. Pralsetinib safety profile in Chinese patients is manageable, 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.

Keywords: Pralsetinib, RET fusion, NSCLC