**Title:** Efficacy and Safety of Pralsetinib, a Selective RET Inhibitor, in Chinese Patients with Advanced RET-mutant Medullary Thyroid Cancer (MTC)

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**Key words:** Pralsetinib, Chinese patients, RET-mutant MTC

***Objective:***

RET mutations are found in about 70% of MTC, yet no targeted therapy was approved or available in China. ARROW is a phase I/II, open-label, multi-cohort study to evaluate the efficacy and safety of pralsetinib in a variety of advanced RET altered solid tumors including MTC. Here we present the results from a phase II cohort of Chinese patients with advanced MTC in ARROW study.

***Methods:***

Patients with advanced or metastatic MTC who were naïve to systemic therapies (except cytotoxic chemotherapies) were enrolled and treated with pralsetinib 400 mg QD. The primary endpoints are the objective response rate (ORR) by blinded independent central review (BICR) per RECIST v1.1 and safety in Chinese patients.

***Results:***

As of 12 April 2021 data cut off, 34 Chinese patients were enrolled and 28 of them were tested as RET mutation-positive by central testing (mutation: 64.3% M918T, 21.4% cysteine-rich domain mutations, 14.3% others). Nearly all (96.4%, 27/28) patients had stage IVC disease at baseline. All patients except one were systemic treatment-naïve . In 26 patients with measurable disease at baseline per BICR, the ORR was 73.1% (95% CI: 52.2, 88.4) with 3 (11.5%) patients achieving complete responses. Disease control rate was 84.6% (95% CI: 65.1, 95.6). The median time to response was 5.75 (range: 1.8-12.8) months. The median duration of response was not reached yet at data cut-off. The 6-month and 9-month DOR rates were both 100%. All RET-mutant patients who received at least 1 dose of pralsetinib were included in the safety analysis (n=28). The most common treatment-emergent adverse events (AEs) were aspartate aminotransferase increased (60.7%), hypocalcaemia (60.7%), hyperphosphataemia (57.1%), white blood cell count decreased (57.1%%), blood lactate dehydrogenase increased (53.6%), and neutrophil count decreased (53.6%). No patients discontinued treatment or died due to treatment-related AEs.

***Conclusions:***

This is the first pivotal study demonstrating the robust, durable antitumor activity and the manageable safety profile of pralsetinib in Chinese patients with RET-mutant MTC. The data are consistent with those previously reported from the global population in ARROW study. Overall, pralsetinib provides a potent targeted treatment and valuable addition to the armamentarium for Chinese patients with RET-mutant MTC.

**Clinical trial identification:** NCT03037385