Abstract 2954

Efficacy and Safety of Pralsetinib in Chinese Patients with Advanced RET Fusion+ Non-Small Cell Lung Cancer after Platinum-Based Chemotherapy

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Introduction

RET fusions have been reported as oncogenic drivers in 1% to 2% of non-small cell lung cancer (NSCLC) patients. Pralsetinib is a highly potent and selective RET kinase inhibitor targeting oncogenic RET alterations. A global phase I/II ARROW study (NCT03037385) has demonstrated broad and durable antitumor activity of pralsetinib in a variety of advanced RET-altered solid tumors. Here we present the efficacy and safety results from the phase II NSCLC extension group that enrolled patients from China sites.

Methods

RET fusion+ Chinese NSCLC patients previously treated with platinum-based chemotherapy were enrolled and dosed with pralsetinib 400 mg QD. The primary objectives were to assess the objective response rate (ORR) by blinded independent central review (BICR) per RECIST v1.1 and safety profile in Chinese patients.

Results

From Aug to Dec 2019, a total of 37 patients were enrolled; most (94.6%) of the patients had ECOG PS of 1 and about half (48.6%) had received ≥3 prior systemic regimens. As of the data cut-off (22 May 2020), 28 patients remained on study treatment and 9 discontinued from pralsetinib (4 due to disease progression and 3 due to adverse events). The median treatment duration was 6.1 (range: 0.9-9.4) months. In 32 evaluable patients who had measurable disease at baseline per BICR, the ORR was 56.3% (95% CI: 37.7, 73.6) (1 complete response [CR] and 17 partial responses [PR]); in addition, 2 patients achieved PR pending confirmation. Clinical benefit rate (defined as the rate of confirmed CR or PR, or stable disease lasting ≥ 16 weeks from the first dose) was 81.3% (95% CI: 63.6, 92.8). Disease control rate was 96.9% (95% CI: 83.8, 99.9), and tumor regression was observed in all 13 patients with stable disease. The median time to response was 1.9 (range: 1.7-5.5) months. Median duration of response (DOR) was not reached; 6-month DOR rate was 83.1% (95% CI: 61.5, 100). All 37 patients experienced at least one treatment emergent adverse event (TEAE). The most frequently reported TEAEs were aspartate aminotransferase increased (83.8%), neutrophil count decreased (70.3%), anaemia (67.6%), white blood cell count decreased (56.8%), and hypertension (51.4%). Grade ≥ 3 TEAEs occurred in 25 (67.6%) patients, with the most common being neutrophil count decreased (24.3%), anaemia (24.3%), hypertension (16.2%), hypophosphataemia (13.5%), platelet

count decreased (10.8%) and hypokalaemia (10.8%). There were no pralsetinib related AEs leading to death.

Conclusion

This is the first pivotal study to show that pralsetinib has deep and durable antitumor activity, and is well-tolerated in a cohort of Chinese patients with RET fusion+ NSCLC previously treated with platinum-based chemotherapy. The data are consistent with previously reported data from the global population in the ARROW trial. Overall, pralsetinib demonstrated a favorable benefit-risk profile, potentially offering a transformative medicine to Chinese RET-fusion driven advanced NSCLC patients.