Clinical activity and safety of the RET inhibitor pralsetinib in patients with RET fusion–positive solid tumors: update from the ARROW trial

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Background and methods

• Rearranged during transfection (RET) fusions are oncogenic drivers in several tumor types.1–10
• Recent RET-agnostic drug approvals have resulted in a paradigm shift in cancer treatment away from organ/histology-specific indications to biomarker-guided tumor-agnostic approaches.11,12
• Pralsetinib is a highly potent, oral, selective RET inhibitor that targets RET alterations, including fusions and mutations, regardless of the tissue of origin.11,14
• Data from the ongoing global phase 1/2 ARROW study (NCT03037385) supported the US FDA approval of pralsetinib once daily (QD) for RET fusion–positive non-small cell lung cancer (NSCLC) and advanced/metastatic RET–altered thyroid cancers.15
• Here we provide an update on the clinical activity of pralsetinib in patients with advanced RET fusion–positive solid tumors other than NSCLC and thyroid cancer ("other" RET fusion–positive solid tumors).16

ARROW study design

Phase 1: Dose escalation (Completed)

• Pralsetinib dosing: 300–600 mg PO QD or BID

Phase 2: Dose expansion (Ongoing)

• Pralsetinib dosing: 400 mg PO QD

Eligibility criteria

• Age ≥18 years
• Advanced or metastatic solid tumor
• RET alteration per local assessment
• Measurable disease (RECIST v1.1)
• ECOG PS 0–1

Data presented for patients enrolled March 17, 2017, to May 22, 2020

Data cut-off November 6, 2020

AE, n (%) 9 (43) 1 (5)
Increased ALT 8 (38) 1 (5)
Neutropenia 7 (33) 6 (29)
Anemia 5 (24) 4 (19)
Fatigue 5 (24) 2 (10)
Hypertension 1 (5) 2 (10)
Thrombocytopenia 1 (5) 2 (10)
Decreased white blood cell count 4 (19) 1 (5)
Constitution 4 (19) 0

Contents of the EPC

AE, n (%)
• Most treatment-related AEs were primarily Grade 1–2
• 1 patient discontinued treatment due to treatment-related AEs
• Overall, 8 patients (38%) had dose reductions due to treatment-related AEs

Conclusions

• Pralsetinib showed robust, durable antitumor activity in patients across a variety of RET fusion–positive, heavily pre-treated, advanced solid tumors
• Pralsetinib was well-tolerated with a safety profile generally consistent with that previously reported in the overall safety population (all tumor types), with no new safety signals
• Over half of (53%) experienced objective tumor responses and tumor shrinkage was observed in 89% of evaluable patients, irrespective of RET fusion partner
• These data highlight the need for broad RET testing to identify candidates who may benefit from treatment with pralsetinib

Enrollment of patients with other RET fusion–positive solid tumors in ARROW is ongoing

References