Background and methods

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Per-protocol patients were evaluable for safety and efficacy. The primary endpoint was ORR per RECIST v1.1 in the modified intent-to-treat (mITT) population. Efficacy analyses included all enrolled patients. The primary safety analysis included all patients treated with pralsetinib. **Protocol amendment July 2019; this amendment expanded inclusion criteria to allow recruitment of treatment-naive patients eligible for standard platinum-based therapy who had ≥3% RET fusion–positive NSCLC**. In total, 216 patients were enrolled in the ARROW study, including treatment-naive patients (n=22) and platinum-naive patients (n=194) who had received prior platinum-based chemotherapy or other standard systemic therapies.

**Key 2° endpoints:**

- Duration of response in treatment-naïve patients
- Duration of response in treatment-naïve patients
- All tumor types
- 26 (12%) of 216 patients discontinued due to AEs (4% of patients stil in treatment) and 9% (44 of 471 patients) discontinued due to disease progression or patient choice

**Safety population, N=471**

- Patients who received pralsetinib at the RPQ of 400 mg QD

** treatment-naïve patients with NSCLC ≥3% RET fusion—positive NSCLC; n=233**

**Other RET-allocated solid tumors; n=238**

- **Pre-eligibility revision**

**Post eligibility revision**

**Protocol amendment July 2019; this amendment expanded inclusion criteria to allow recruitment of treatment-naïve patients eligible for standard platinum-based therapy who had ≥3% RET fusion–positive NSCLC.**

**Results**

- **Tumor shrinkage in patients with prior platinum-based chemotherapy**

**Duration of response in treatment-naïve patients**

- **Duration of response in treatment-naïve patients**

**Conclusions**

- Pralsetinib is a well-tolerated once-daily oral treatment option for patients with RET fusion–positive metastatic NSCLC, with a safety profile consistent with previous reports and no new safety signals.

- With a longer overall follow-up (17.1 months vs 8.8 months in previous analysis), pralsetinib showed durable responses across all RET fusion–positive NSCLC treatment groups.

- Notably, 88% was in the post-eligibility revision subset, which included treatment-naïve patients who were otherwise eligible for standard platinum-based therapy.

- These data support the importance of early biomarker testing for all patients with metastatic NSCLC prior to treatment initiation to inform optimal healthcare decisions.

- Pralsetinib is currently approved for the treatment of metastatic RET fusion–positive NSCLC and advanced or metastatic RET-altered thyroid cancers in the USA, and is locally advanced or metastatic NSCLC after platinum-based chemotherapy in China.

**References**

- Dr. Giuseppe Curigliano has a consulting or advisory role with the following: AstraZeneca, BMS, Boehringer, Daiichi Sankyo, Foundation Medicine, GlaxoSmithKline, Lilly, Novartis, Pfizer, Roche/Genentech, Samsung, and Seattle Genetics. Speakers Bureau: Daiichi Sankyo, Foundation Medicine, Lilly, Novartis, Pfizer, Roche/Genentech, and Seattle Genetics.

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**Tests for Adverse Events**

- Common Terminology Criteria for Adverse Events (CTCAE) version 5.0

**Tests for Tumor Response**

- RECIST v1.1

**Additional analyses**

- **Tumor shrinkage in patients with prior platinum-based chemotherapy**

- **Duration of response in treatment-naïve patients**

- **Duration of response in treatment-naïve patients**

- **Safety population, N=471**

- **Patients who received pralsetinib at the RPQ of 400 mg QD**

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