AcceleRET Lung: a phase 3 study of first-line pralsetinib in patients with RET fusion–positive advanced/metastatic NSCLC

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BACKGROUND

Rearranged during transfection (RET) gene fusions have been identified as oncogenic drivers in multiple tumor types, including 1–2% of non-small-cell lung cancer (NSCLC)2,3. Patients with RET alterations have poor response to immunotherapies, but those with NSCLC bearing certain driver mutations have shown improved outcomes with targeted therapy compared with standard of care (SOC) platinum-based chemotherapy4,5. Pralsetinib is a RET inhibitor that selectively targets RET fusions and mutations, with greater potency than multikinase inhibitors6,7. In the phase 1/2 ARROW study (NCT03037385; data cutoff: November 6, 2020), pralsetinib demonstrated an overall response rate of 79% in treatment-naive patients with RET fusion–positive metastatic NSCLC (n=68) and substantial antitumor activity (Figure 1)8. Across the entire safety population (N=471) in the ARROW study, the most common treatment-related adverse events were of grade 1–2 per the Common Terminology Criteria for Adverse Events (CTCAE)9.

Pralsetinib was approved by the US Food and Drug Administration (FDA) for the treatment of adult patients with RET fusion–positive metastatic NSCLC as detected by an FDA-approved test, and by the European Commission for the treatment of adult patients with RET fusion–positive advanced NSCLC not previously treated with a RET inhibitor10,11.

Figure 1: Pralsetinib demonstrated substantial antitumor activity in treatment-naive patients with RET fusion–positive metastatic NSCLC in the phase 1/2 ARROW study8.

METHODS

Study objectives and design

AcceleRET Lung, an international, open-label, randomized, phase 3 study (NCT04222972), will evaluate the efficacy and safety of pralsetinib compared with investigator’s choice of platinum-based chemotherapy regimen as first-line treatment in patients with RET fusion–positive metastatic NSCLC.

Patients will be randomized 1:1 to receive pralsetinib 400 mg once daily or investigator’s choice of SOC treatment (Figure 2). Stratification factors include intended presence of brain metastasis, Eastern Cooperative Oncology Group performance status, and intended use of pembrolizumab if randomized to the SOC arm. Crossover to receive pralsetinib will be allowed for patients randomized to SOC upon disease progression confirmed by central review assessment.

Figure 2: AcceleRET lung study design

Summary of key eligibility criteria

Key inclusion criteria

- Adult patients aged ≥18 years
- Pathologically confirmed advanced or metastatic NSCLC
- Measurable disease (RECIST 1.1) as determined by local site investigator or radiologic assessment
- Documented RET fusions as assessed by an accredited laboratory
- ECOG PS of 0–1
- Prior therapy in the neo/adjuvant setting is allowed if recurrence occurred after 6 months from completion of treatment

Key exclusion criteria

- Prior systemic treatment for metastatic disease
- Tumor has an additional primary targetable driver mutation
- Prior treatment with a selective RET inhibitor
- CNS metastases or primary CNS tumor associated with progressive neurological symptoms

Figures

Figure 3: Active study sites

ENROLLMENT AND CURRENT STATUS

- The target enrollment is 226 patients
- Enrollment in this international multicenter study is planned/has begun in 128 sites in 21 countries including North America, Europe, Asia, and Australia (Figure 3)

Figure 3: Active study sites


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