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

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Disclosures

Commercial Interest	Relationship(s)
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Pralsetinib is approved by the US Food and Drug Administration (FDA) for the treatment of adults with metastatic *RET* fusion–positive non-small cell lung cancer, and for the treatment of adult and pediatric patients (aged ≥12 years) with advanced or metastatic *RET*-mutant medullary thyroid cancer who require systemic therapy or *RET* fusion–positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

Pralsetinib is not approved for the treatment of any other indication in the USA by the FDA or for any indication in any other jurisdiction by any other health authority.

Background

- Activating alterations in the *RET* receptor tyrosine kinase gene are oncogenic drivers in multiple solid tumors, including 1–2% of NSCLC[1,2]
- Patients with *RET* alterations have poor response to immune checkpoint inhibitor therapy[3,4]
- In patients with NSCLC and other oncogenic driver alterations, targeted therapies have shown improved outcomes compared with SOC platinum-based chemotherapy[5,6]
- *In vitro*, pralsetinib selectively targeted *RET* with oncogenic alterations with greater potency than multikinase inhibitors[7], and was recently approved by the US FDA for the treatment of adult patients with metastatic *RET* fusion–positive NSCLC[8]
- Pralsetinib is also approved for the treatment of adult and pediatric patients (aged ≥12 years) with advanced or metastatic *RET*-mutant medullary thyroid cancer or *RET* fusion–positive thyroid cancer in the US[8]

FDA, Food and Drug Administration; NSCLC, non-small cell lung cancer; RET, rearranged during transfection; SOC, standard of care.

1. Kohno T et al. *Nat Med.* 2012;18:375–377; 2. Lipson D et al. *Nat Med.* 2012;18:382–384; 3. Mazieres J et al. *Ann Oncol.* 2019;30:1321–1328; 4. Tufman A et al. *J Clin Oncol.* 2018;36:15(suppl):e21071;
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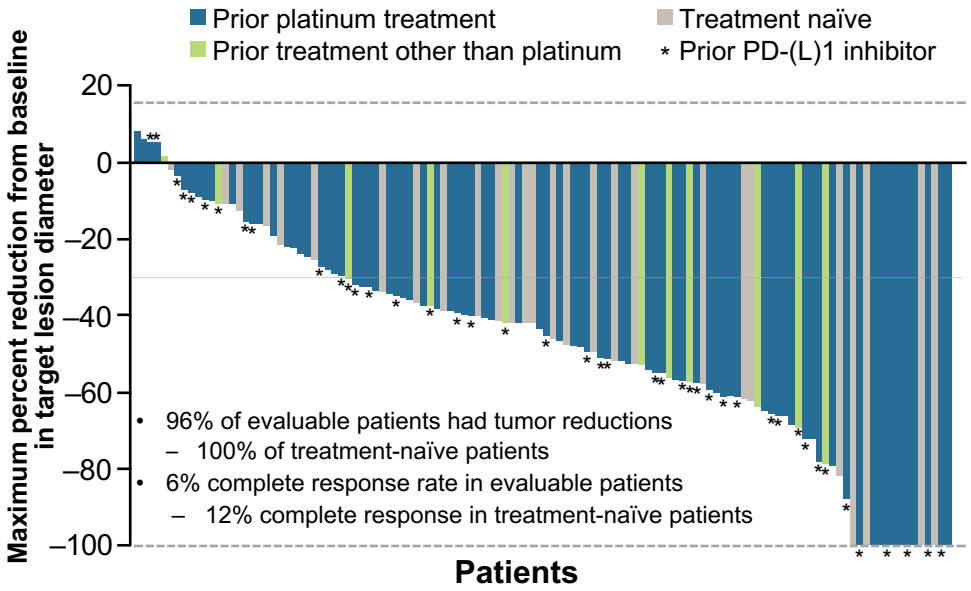
8. Blueprint Medicines Corporation. GAVRETO™ (pralsetinib). Prescribing information. 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214701s000lbl.pdf. Accessed December 2, 2020.

Background

- In the registration-enabling phase 1/2 ARROW study (**NCT03037385**), pralsetinib showed:[1,a]
  - ORR of 61% in adult patients with metastatic *RET* fusion–positive NSCLC in patients previously exposed to platinum-based therapy (n=80)
  - ORR of 73% with a 12% complete response rate as first-line treatment (n=26)
  - The majority of treatment-related adverse events were Grade 1–2 across the entire safety population (irrespective of tumor type)

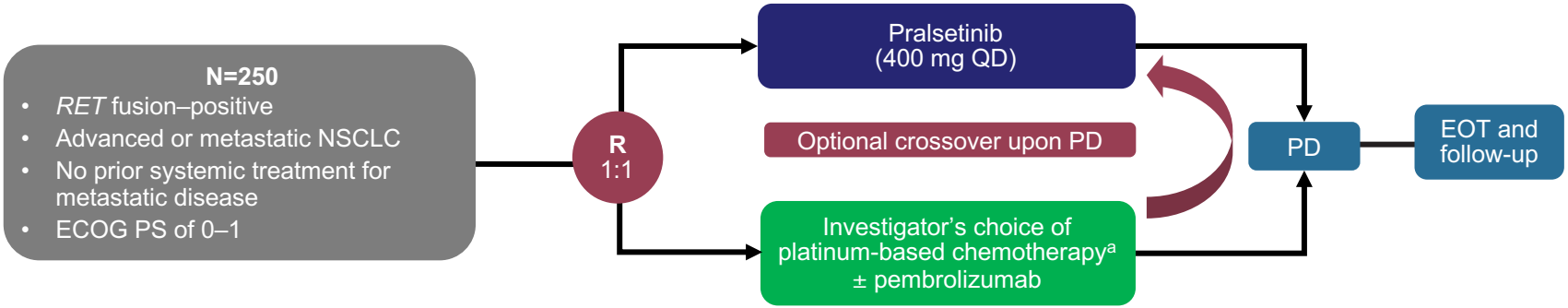
All *RET* fusion–positive NSCLC response-evaluable patients (400 mg QD) per blind independent centralized review



[a]Data cut-off November 18, 2019.
ORR, overall response rate; PD-L(1), programmed death-ligand 1; QD, once daily.
1. Gainor JF, et al. Presented at the Annual Meeting of the American Society of Clinical Oncology, May 29–Jun 2, 2020, virtual format.

AcceleRET Lung

- **International, open-label, randomized, phase 3 study (NCT04222972) in patients with *RET* fusion–positive NSCLC**
- **Efficacy and safety of pralsetinib vs investigator's choice of platinum-based chemotherapy regimen as first-line treatment**



- Stratification factors include intended pembrolizumab use if randomized to the investigator's choice arm, history of brain metastases, and ECOG PS
- Crossover to receive pralsetinib will be allowed for patients randomized to the investigator's choice arm upon PD confirmed by central review assessment

[a]Patients with non-squamous histology will receive platinum/pemetrexed with or without pembrolizumab; patients with squamous histology will receive platinum/gemcitabine.
ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; PD, progressive disease; R, randomized.

Key eligibility

Inclusion criteria

- Adult patients aged ≥18 years
- Pathologically confirmed advanced or metastatic NSCLC
- Measurable disease (RECIST v1.1) determined by local site investigator or central radiographic imaging review assessment
- Documented *RET* fusions assessed in tissue or plasma per local site assessment or in tumor tissue assessed by central NGS-based assay
- ECOG PS of 0–1
- Prior therapy in the neoadjuvant or adjuvant setting is allowed if recurrence occurred after ≥6 months from completion of treatment

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 associated with progressive neurological symptoms
- Primary CNS tumor associated with progressive neurological symptoms

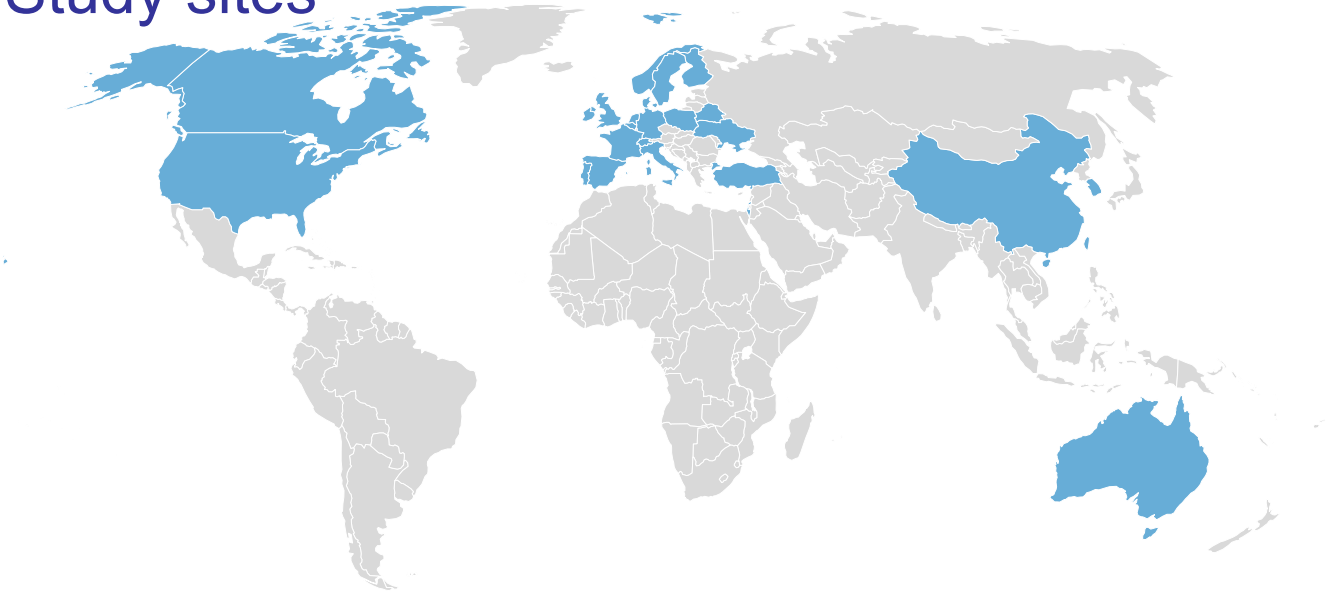
CNS, central nervous system; NGS, next generation sequencing; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Study endpoints

Primary endpoint	**Progression-free survival** compared with investigator's choice of SOC treatment according to a blinded independent central review (RECIST v1.1) • Sample size (N=250) determined based on the assumption of a 0.57 hazard ratio for pralsetinib vs investigator's choice of SOC treatment	
Secondary endpoints	• ORR[a] • Overall survival • Safety/tolerability • Clinical benefit rate[b] • Duration of response[a] • Disease control rate[c]	• Time to intracranial progression[a] • Intracranial response rate[a] • Quality-of-life measurements[d] • Pharmacokinetics

[a]Per RECIST v1.1; [b]Defined as the proportion of patients who experience a best response of stable disease (SD) with a minimum duration of 16 weeks a complete response (CR), or a partial response (PR) according to RECIST v1.1; [c]Defined as the proportion of patients who experience a best response of CR, or PR, or SD according to RECIST v1.1; [d]European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30-question, the EORTC Quality of Life Questionnaire-Lung Cancer 13, and the EuroQoL 5 Dimension questionnaires.

Study sites



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	Poland
	Portugal
	Spain
	Sweden
	Switzerland
	Turkey
	Ukraine
	United Kingdom

- AcceleRET Lung target enrollment is 250 patients in 26 countries. Overall, 73 sites are actively enrolling patients and ~140 sites are planned globally
- Contact medinfo@blueprintmedicines.com for more information on study sites and enrollment

EMEA, Europe, the Middle East, and Africa.

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