Encorafenib plus binimetinib in patients with BRAF^{V600}-mutant non-small cell lung cancer: Phase II PHAROS study design

Authors: Gregory J Riely, Myung-Ju Ahn, Enriqueta Felip, Suresh S Ramalingam, Egbert F Smit, Anne S Tsao, Ann Alcasid, Tiziana Usari, Paul S Wissel, Keith D Wilner & Bruce E Johnson

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Objective and rationale

Primary objective

Evaluate the antitumor activity of encorafenib plus binimetinib in treatment-naïve and previously treated patients with BRAF^{V600}-mutant NSCLC as measured by ORR and determined by IRR

Rationale

BRAF/MEK combination therapy is approved in BRAF^{V600}-mutant NSCLC, and encorafenib plus binimetinib has shown a manageable safety profile and antitumor activity in patients with metastatic melanoma

Study design

On-study treatment

- Open label
- Single arm
- P2: Patients with BRAF^{V600}-mutant NSCLC who had received no more than 1 prior treatment in the advanced setting

Eligible patients receive encorafenib 450 mg QD plus binimetinib 45 mg BID orally until disease progression, unacceptable toxicity, withdrawal of consent, initiation of subsequent anticancer therapy, death or end of study

- Approximately 107 patients are planned to be enrolled
  - At least 60 treatment-naïve and 37 previously treated patients with BRAF^{V600E} mutation
  - Up to 10 additional patients with other BRAF^{V600} mutations may also be included

Outcome measures

Primary endpoint

Confirmed ORR as determined by IRR per RECIST v1.1 in treatment-naïve and previously treated patients

Key secondary endpoints

Confirmed ORR by the investigator per RECIST v1.1
DOR (by IRR and investigator)
TTR (by IRR and investigator)*
DCR (by IRR and investigator)
PFS (by IRR and investigator)
OS
Safety

*Endpoint will be analyzed but was not prespecified in the study protocol

Key eligibility criteria

Key inclusion criteria

NSCLC, Stage IV
Metastatic disease

BRAF^{V600E}-positive†
Identified in tumor tissue or blood, as determined by PCR or NGS-based local laboratory assay
†Other less common Class 1 BRAF^{V600} mutations (eg, K or D) permitted with prior discussion with the Sponsor

Treatment-naïve or previously treated‡
‡Prior first-line platinum-based chemotherapy or prior first-line anti-PD-1/PD-L1 inhibitor treatment (alone or in combination with another immunotherapy and/or platinum-based chemotherapy)

≥18 years old
Have measurable disease per RECIST v1.1, an ECOG PS of 0–1 and adequate tumor tissue for submission to central laboratory for confirmation of mutation status

Key exclusion criteria

Documented EGFR mutation, ALK fusion oncogene or ROS1 rearrangement

Symptomatic CNS involvement

Prior treatment with any BRAF or MEK inhibitor

Active non-infectious pneumonitis or history of ILD

Glossary: *BID: Twice daily; CNS: Central nervous system; DCR: Disease control rate; DOR: Duration of response; ECOG PS: Eastern Cooperative Oncology Group performance status; ILD: Interstitial lung disease; IRR: Independent radiology review; NGS: Next-generation sequencing; NSCLC: Non-small cell lung cancer; ORR: Objective response rate; OS: Overall survial; PCR: Polymerase chain reaction; PFS: Progression-free survival; QD: Once daily; RECIST: Response Evaluation Criteria in Solid Tumors; TTR: Time to tumor response*

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