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A Dose Exploration Study of Almonertinib for Epidermal Growth Factor Receptor (EGFR)-Mutant Non-small-cell Lung Cancer (NSCLC) Patients With Newly Diagnosed or Recurrent Brain/leptomeningeal Metastasis (ARTISTRY)

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BACKGROUND

- Approximately 25-40% of patients with NSCLC have brain metastases (BM) and 3-4% develop leptomeningeal metastases (LM)[1,2]. The prognosis of patients with BM or LM is dismal, which seriously affects the quality of life (QoL) and survival of patients
- The FLAURA and BLOOM trials[3,4] suggested there may be a role for 3rd generation EGFR-TKI in the treatment of EGFR-mutant NSCLC patients with BM and/or LM
- Almonertinib (HS-10296) is a novel 3rd generation EGFR-TKI with high capability to penetrate the blood-brain barrier. In the phase I dose-escalation trial with the highest dose at 260mg/d, maximum tolerated dose (MTD) of Almonertinib has not been reached[4]
- In the phase II APOLLO trial, almonertinib exhibited good control over BM in EGFR-mutant NSCLC patients: the CNS ORR was 60.9% (95% CI: 38.5, 80.3), the CNS mPFS (48.0% maturity) was 10.8 (95%CI: 9.6, 13.8) months[5]

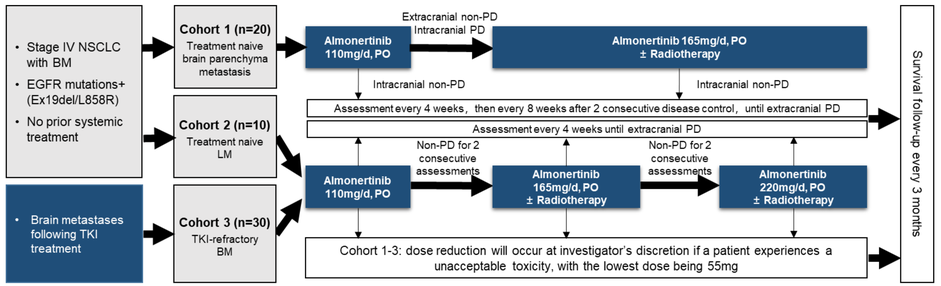
RATIONALE

- For the first time to observe the efficacy and safety of almonertinib in the treatment of EGFR-mutant NSCLC patients with BM and/or LM in a real-world environment
- To explore more accurate and individualized treatment between newly diagnosed and recurrent EGFR-mutant NSCLC patients with BM and/or LM
- Balancing the efficacy and safety to maximize the benefits for patients

CNS REAL WORLD STUDY DESIGN

- ARTISTRY (NCT04778800) is a prospective, open-label, single-arm, single-center, three-cohorts study in EGFR-mutant NSCLC patients with BM and/or LM
  - Cohort 1: Treatment naïve patients with brain parenchyma metastasis (n=20)
  - Cohort 2: Treatment naïve patients with leptomeningeal metastasis (n=10)
  - Cohort 3: Patiens with intracranial progression on prior 1st or 2nd generation EGFR-TKI therapy (n=30)
- For cohort1, patients will receive oral almonertinib 110mg/d once daily. The dose will be escalated to 160mg/d if intracranial PD and no extracranial PD is observed. Assessments are to be performed every 4 weeks and then every 8 weeks until extracranial PD as per RECIST v1.1
- For cohort 2&3, patients will receive oral almonertinib 110/160/220mg/d once daily. The dose escalation continues if no PD is observed in 2 consecutive assessments. Assessments are to be performed every 4 weeks until extracranial PD as per RECIST v1.1

Figure 1. ARTISTRY Study Design



- **Primary Endpoint:** Intracranial PFS (iPFS)
- **Secondary Endpoints:** PFS, OS, DCR, iORR, iDoR, Safety

BACKGROUND

Key inclusion criteria

- Male or female, age ≥18 years old
- Histologically confirmed NSCLC with BM (including patients who have relapsed after previous treatment or newly diagnosed)
- For Cohort 1&3: at least one measurable intracranial lesion and not previously irradiated at the time of enrollment
- For Cohort 2: patients who experienced dizziness/headache with positive CSF cytology or clear leptomeningeal enhancement on MRI
- For Cohort 1&2: patients who had not received other systemic therapy after the diagnosis of stage IV NSCLC
- For Cohort 3: patiens with intracranial progression or intracranial lesions that have not achieved response on prior 1st or 2nd generation EGFR-TKI therapy
- Tumor tissue samples or blood are confirmed to be EGFR sensitive mutations (Ex19del/L858R) by ARMS
- ECOG PS is 0-2 and has not deteriorated in the previous 2 weeks, with a minimum expected survival of 12 weeks
- Measurable extracranial disease is not required; if there is, the lesions are required to be accurately measured at baseline as ≥10 mm in the longest diameter (except lymph nodes which must have a short axis of ≥15 mm) with CT or MRI

Key exclusion criteria

- Judgment by the Investigator that the risk to patients is likely higher than the benefit after enrollment
- Is currently participating in any other clinical trials
- Any concurrent and/or other active malignancy
- History of hypersensitivity to any active or inactive ingredient of almonertinib or to drugs with a similar chemical structure or class to almonertinib
- Women who are pregnant or breastfeeding

STATISTICAL ANALYSIS

- Continuous data will be summarized using descriptive statistics (mean, SD, min, max)
- Categorical (discrete) data will be summarized using frequencies and percentages
- Time-to-event data will be summarized with the exact 95% confidence interval per the Kaplan-Meier method

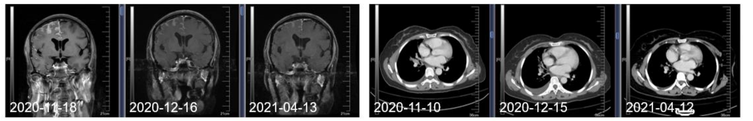
STUDY STATUS

- Estimated study duration: 2020.10.01 - 2023.10.01
- At present, 12 patients have been enrolled

TYPICAL CASE

- A female patient, 53 years old, no history of smoking
- Enrolled in Nov, 2020
- Diagnosis: Primary stage IVB right lung adenocarcinoma (cT4N3M1c) with bone, brain, leptomeningeal metastases, EGFR ex19del and L858R
- Treatment: Almonertinib 110mg/d, PO

Figure 2. Brain MRI and Chest CT before and after treatment



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ABBREVIATION:

NSCLC, non-small cell lung cancer; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitors; ORR, objective response rate; PFS, progression free survival; CNS, central nervous system; PD, progression disease; OS, overall survival; DCR, disease control rate; DoR, duration of response; CSF, cerebrospinal fluid; ECOG PS, eastern cooperative oncology group physical status score; CT, computed tomography; MRI, magnetic resonance imaging; SD, standard deviation.

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