Trial in progress: A phase 1/2a trial of Aurora-A inhibitor (JAB-2485) in adult patients with advanced solid tumors

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Background

- Aurora kinase A (AURKA), a crucial mitotic regulator, is frequently dysregulated in a wide range of cancers, which contributes to clinical aggressiveness and poor patient survival, making it an attractive therapeutic target.
- Prior studies with pan-Aurora kinase inhibitors have shown limited success, largely owing to the narrow therapeutic window associated with bone marrow toxicity caused by targeting Aurora B. The development of highly selective AURKA inhibitors, with improved efficacy and tolerability, is highly warranted.
- JAB-2485, a potent, small-molecule AURKA inhibitor with greater than 1500-fold selectivity over AURKB and AURKC, may efficiently induce G2/M phase cell cycle arrest (Figure 1) and apoptosis of cancer cells *in vitro*. Furthermore, it showed impressive anti-tumor efficacy both as a single agent and in synergy with chemotherapies in multiple animal models. [1]

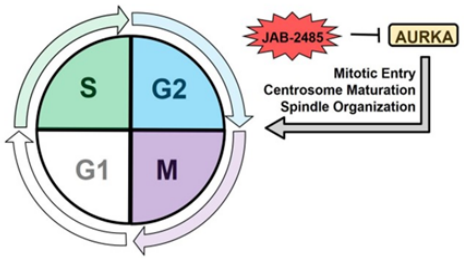

Figure 1 Mechanism of JAB-2485, a potent, small-molecule AURKA inhibitor

Aim of the Trial

This global first-in-human, open-label, multi-center phase 1/2a trial evaluates the safety, tolerability, pharmacokinetics, and preliminary evidence of antitumor activity of JAB-2485 in adult patients with advanced solid tumors.

Key Inclusion Criteria

- Must have Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1
- Must be able to provide an archived tumor sample
- Must have histologically or cytologically confirmed metastatic or locally advanced solid tumor
  - Dose Expansion phase cohorts must meet specific expression or gene mutation where indicated
- Must be refractory to or become intolerant of existing therapy(ies) known to provide clinical benefit for their condition
- Must have at least 1 measurable lesion per RECIST v1.1
- Must have adequate organ functions
- Must be able to swallow and retain orally administered medication

Key Exclusion Criteria

- Has brain or spinal metastasis, except if treated and no evidence of radiographic progression or hemorrhage for at least 28 days
- Active infection requiring systemic treatment within 7 days of the first study treatment in this trial
- Active hepatitis B virus (HBV), or hepatitis C virus (HCV)
- Known human immunodeficiency virus (HIV) infection or positivity on immunoassay
- Any severe and/or uncontrolled medical conditions
- Left ventricular ejection fraction (LVEF) ≤50% assessed by echocardiogram (ECHO) or multigated acquisition scan (MUGA)
- QT interval using Fridericia's formula (QTcF) >470 msec
- History of clinically significant eye disorders

Study Endpoint

Primary endpoint: The incidence of dose-limiting toxicity (DLT) and the safety and tolerability of JAB-2485.

Secondary endpoints: Pharmacokinetics, overall response rate, time to response, and duration of response.

Exploratory endpoints: Correlative pharmacodynamic markers.

Trial Design

In the dose escalation phase (phase 1), six dose levels of daily JAB-2485 (5, 10, 20, 40, 60, and 80mg) will be explored to determine the maximum tolerated dose (MTD) using a modified toxicity probability interval 2 (mTPI-2) method. After determining the recommended phase 2 dose (RP2D), the dose-expansion phase (Phase 2a) will explore the preliminary anti-tumor activity of JAB-2485 as a single agent in patients with ER+ breast cancer, triple-negative breast cancer, small cell lung cancer, and tumors harboring *ARID1A* mutations (Figure 2).

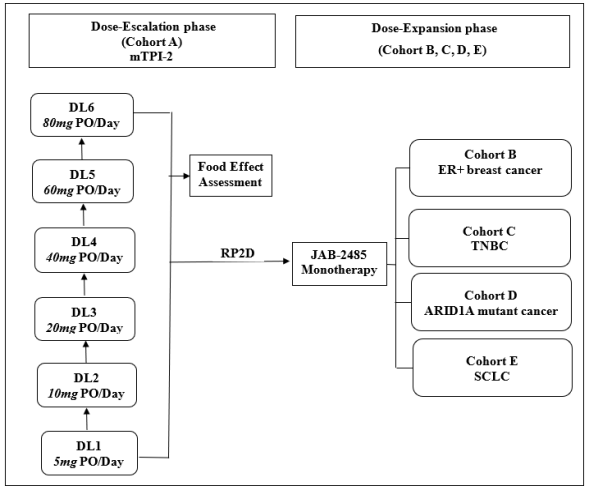

Figure 2 Study Design Schema (DL = dose level; n = number of participants; SCLC = small cell lung cancer; PO = by mouth; RP2D = recommended Phase 2 dose; TNBC= triple negative breast cancer)

Enrollment and Participating countries

- Enrollment in this trial started in January 2023 in the US and April 2024 in China.
- Approximately 102 patients will be enrolled.
- Patients will be enrolled across 6 cities at 2 countries (Figure 3)
- Participating cities: Dallas, Salt Lake City, Detroit, Beijing, Changchun, and Jinan

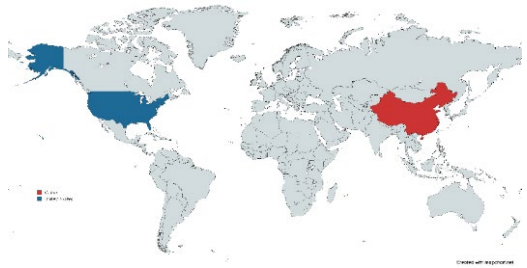

Figure 3 Participating countries (Created with mapchart net)

References

1. Yang G, et al. *ACS Omega.* 2024;9:21416-21425.

Study Contact

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Sponsor

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Disclosure

The first and presenting author Vaia Florou has the following relationships to disclose: Consulting/advisory board roles with Deciphera, Springwork Therapeutics, and Aadi Bioscience.

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Further information on this trial can be found at: Study Details | JAB-2485 Activity in Adult Patients With Advanced Solid Tumors | ClinicalTrials.gov

Clinical trial information: NCT05490472/CTR20223395