Title: A Phase 1b Safety and Dose-Finding Clinical Trial of an Investigational Drug for Advanced Pancreatic Cancer

Introduction:
This phase 1b clinical trial evaluates the safety and dose-limiting toxicities of a novel investigational drug, AB-201, in patients with advanced pancreatic cancer. AB-201 is a first-in-class small molecule designed to inhibit a specific cellular pathway implicated in tumor growth. Preclinical studies have shown promising anti-tumor activity and a favorable safety profile.

Methods:
The dose-escalation trial enrolled patients with unresectable or metastatic pancreatic cancer who had progressed after first-line therapy. Patients received oral AB-201 once daily in 28-day treatment cycles. Starting doses were determined based on preclinical data, and dose cohorts were incrementally increased until the maximum tolerated dose (MTD) was established.

Safety assessments included adverse event monitoring, clinical laboratory evaluations, vital sign measurements, and physical examinations. The Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 was used for toxicity grading.

Results:
The trial enrolled 24 patients, and the drug was generally well tolerated. No dose-limiting toxicities were observed up to the 200 mg dose level. The most common adverse events were grade 1-2 and included fatigue, nausea, and diarrhea. These side effects were manageable and typically resolved within a few days without permanent discontinuation of the drug.

Two patients experienced grade 3 adverse events, including elevated liver enzymes and neutropenia, both of which resolved with dose reduction and supportive care. No grade 4 or higher adverse events, treatment-related serious adverse events, or deaths occurred during the trial.

Based on the safety data, the MTD was determined to be 200 mg. A subsequent expansion cohort of 12 patients was treated at this dose level, further confirming its safety.

Pharmacokinetic Analysis:
Pharmacokinetic evaluations demonstrated that AB-201 exhibited linear kinetics with dose escalation. The drug's half-life was consistent with the once-daily dosing schedule, allowing for convenient administration. No significant drug interactions or alterations in vital signs were observed.

Discussion:
The results indicate that AB-201 has an acceptable safety profile at the recommended phase 2 dose (RP2D) of 200 mg. The absence of dose-limiting toxicities and manageable adverse events at this dose supports further investigation of AB-201 in phase 2 trials for advanced pancreatic cancer.

Although the current study focused on safety, preliminary efficacy analyses showed encouraging signs of anti-tumor activity, with three patients achieving stable disease for over six months.

Conclusion:
This phase 1b trial confirms that AB-201 is a well-tolerated and promising treatment option for advanced pancreatic cancer patients. The safety profile, along with the observed anti-tumor activity, warrants the initiation of phase 2 studies to evaluate the drug's efficacy and optimal dosing regimen.

Clinical Trial Registration: NCT04133492