



January 19, 2018
J-Pharma Co., Ltd.

Completion of Phase I clinical trial of novel anti-cancer agent JPH 203

J-Pharma completed First-in-human Phase I study of JPH203 in patients with advanced solid tumors and Dr. Naohiro Okano, M.D. Assistant Professor, Department of Internal Medicine, Medical Oncology School of Medicine Kyorin University reported the result at American Society of Clinical Oncology Gastrointestinal Cancers Symposium (“ASCO GI”) held at San Francisco January 18 – 20, 2018.

Following is the Abstract of the report uploaded at the site of ASCO GI.

Title: First-in-human Phase I study of JPH203 in patients with advanced solid tumors.

Presented Friday, January 19, 2018

Authors:

Naohiro Okano, Kirio Kawai, Yoshiya Yamauchi, Takaaki Kobayashi, Daisuke Naruge, Fumio Nagashima, Hitoshi Endou, Junji Furuse; Kyorin University, Tokyo, Japan; J-Pharma, Kanagawa, Japan

Abstract Disclosures

Background:

Uptake of amino acids is essential for cancer growth. L-type amino acid transporter-1 (LAT-1) is overexpressed in various cancers, and uptake of LAT-1 substrate amino acids is known to have a critical role in cancer growth. JPH203 is a novel, selective, LAT-1 inhibitor. A first-in-human phase I study of JPH203 was designed to determine the safety, maximum-tolerated dose (MTD) and recommended dose. This study included evaluation of the anti-tumor effect, pharmacokinetics, and pharmacodynamics of JPH203 and analyzed plasma free amino acids.

Methods:

JPH203 was administered intravenously for 7 days followed by 21 days' rest at planned doses ranging from 12 to 110 mg/m² in patients with advanced solid tumors refractory to standard therapy. Before starting this schedule, we confirmed safety of a single dose of JPH203. Dose-limiting toxicity was evaluated during the first cycle, using a 3+3 design.

Results:

17 patients were enrolled from January 2015 to August 2016. One patient was discontinued after a single dose of JPH203 because of tumor progression. Dosage was escalated up to 85 mg/m². Grade 3 liver dysfunction occurred in 1 of 6 patients at 60 mg/m² and in the first patient at 85 mg/m². Therefore, it was determined that MTD was 60 mg/m². Common treatment-related adverse events were increased ALT/AST, malaise, nausea, hypertension and fever of Grade 1 or 2. Partial response was achieved in a patient with biliary tract cancer (BTC) who continued JPH203 for two years without progression. Disease control (PR+SD) was observed in 3 of 5 patients with BTC and 2 of 6 with colorectal cancer. LAT-1 substrate amino acids and branched chain amino acids including LAT-1 substrate amino acids were higher in patients with BTC than in those with other cancers. All patients with disease control had a body mass index more than the median of 20.5 kg/m². In exploratory analysis, longer survival was achieved in patients with high inhibition of uptake of LAT-1 substrate amino acids, compared with patients with low inhibition of uptake.

Conclusions:

JPH203 was well tolerated, resulting in promise against BTC. This phase I study suggested that LAT-1 could be targeted in treatment for advanced BTC, because LAT-1 substrate amino acids in plasma tended to remain high. Clinical trial information: UMIN000016546.

=====