1708PD | MOLECULAR PROFILE AND ANTI-TUMOR ACTIVITY IN NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS (PTS) IN A PHASE 1 STUDY OF CABOZANTINIB (XL184) IN JAPAN

H. Nokihara[1], N. Yamamoto[1], S. Nakamichi[1], H. Wakui[1], Y. Yamada[1], J. Frye[2], A. Decillis[2], T. Tamura[1]

[1]Tokyo/JP, [2]South San Francisco, CA/US

Background

Cabozantinib is a potent targeted therapy that inhibits MET, VEGFR2, and RET. Anti-tumor activity in patients (pts) has been observed in a broad range of tumors including NSCLC. The primary objective of this phase 1 study is to determine the maximum tolerated dose (MTD) / recommended phase 2 dose in Japanese pts.

Methods

Pts with advanced solid malignancies are enrolled in successive cohorts to receive escalating doses of cabozantinib orally once daily in a 3 + 3 trial design. Dose limiting toxicities (DLTs) are determined using Cycle 1 data. Response is assessed using modified RECIST v1.0. Results: As of 1 June 2012, 14 pts were enrolled including 5 pts with non-small cell lung adenocarcinoma. Pts have been treated at 3 dose levels: 40, 60 and 80 mg. The NSCLC pts had a median of 4 prior regimens (range, 2 – 6). Four of the 5 NSCLC pts had a confirmed partial response (cPR) including a 51 yo female whose pre-treatment tumor sample lacked an EGFR activating mutation Analysis of tumor obtained pre-treatment and at progression demonstrated a KIF5B-RET fusion.

Age	Gender	Smoking History	Molecular Profile	Treatment Duration (mos)	Best Response
64	Female	Never	EGFR mutation	15+	cPR
51	Female	Former	EGFR wt, RET fusion positive	9	cPR
58	Female	Never	EGFR wt	10	cPR
43	Male	Former	ALK fusion positive	4	cPR
64	Female	Never	EGFR wt, ALK fusion negative	6.5	SD

DLT of Grade 3 hypertension was reported in 2 pts. The MTD using a capsule formulation is 60 mg. Adverse events were generally mild to moderate and include hypertension, palmar-plantar erythrodysesthesia, diarrhea, mucositis, rash, edema and headache. Laboratory abnormalities include elevated AST/ALT, lipase and TSH; and neutropenia and thrombocytopenia. Preliminary PK analysis showed that dose-normalized exposure in Japanese pts is approximately 2-fold higher than in non-Japanese pts. Despite relatively higher exposures, cabozantinib 60 mg daily appears to be a well tolerated dose. Conclusions: Cabozantinib appears well tolerated. Signs of antitumor activity include response and prolonged stable disease in NSCLC pts. Accrual and additional molecular characterization is ongoing.

Disclosure

H. Nokihara: Taiho Pharmaceutical Co., Ltd, Merck Serono, Pfizer. N. Yamamoto: Chugai

pharmaceutical co., ltd., Pfizer, Kyowa-Hakko Kirin co., ltd. Y. Yamada: Bayer, Yakult, AstraZeneca. J. Frye: Paid employee of Exelixis Exelixis stock ownership. A. Decillis: Paid Employee of Exelixis Exelixis Stock Ownership. T. Tamura: Chugai Pharmaceutical co., ltd., Daichi-Sankyo co., ltd., Boehringer Ingelheim, Abbott Japan Co., Ltd, Eisai co., ltd., Bristol-Myers Squibb, Kyowa-Hakko Kirin co., ltd. All other authors have declared no conflicts of interest.

Session Info: Poster Discussion, [] Developmental therapeutics
Day/Date: Sunday, September 30, 2012
Session Time: 1:00 PM - 2:00 PM
Room: Hall H