739P | PHASE 1 EXPERIENCE OF TIVANTINIB IN PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC) OR BILIARY TRACT CANCER (BTC)

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Background

Tivantinib is a selective MET inhibitor that is extensively metabolized by the liver. Since 2006, > 700 cancer patients (pts) have been treated with tivantinib. Herein we summarize safety, pharmacokinetic (PK), and efficacy data for pts with HCC or BTC treated with tivantinib in phase 1 clinical trials.

Methods

Adverse events (AEs) were assessed using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Tumor responses were assessed via Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. PK parameters were calculated using blood samples collected on day 1 and on day 2 or day 15 of cycle 1.

Results

53 pts (median age, 63 y) with HCC (n = 42; 79%), cholangiocarcinoma (n = 10; 19%), or gallbladder adenocarcinoma (n = 1; 2%) were included. Of these, 23 pts (43%) received tivantinib monotherapy, and 30 pts (57%) received tivantinib in combination with sorafenib (n = 20; 38%), gemcitabine (n = 8; 15%), or erlotinib (n = 2; 4%). Starting tivantinib BID doses were < 240 mg in 3 (6%), 240 mg in 11 (21%), and 360 mg in 39 (74%) pts. Common treatment-emergent AEs (≥ 15% of pts) were fatigue and anemia (45% each); diarrhea (40%); neutropenia and anorexia (38% each); asthenia (30%); thrombocytopenia, peripheral edema, pyrexia, and nausea (25% each); hyperbilirubinemia (23%); vomiting and alopecia (21% each); rash (19%); leukopenia (17%); and palmar-plantar erythrodysesthesia syndrome, dyspnea, and ascites (15% each). Tivantinib PK analysis indicated peak plasma levels 2 h after oral administration (range, 1-6 h). Tivantinib exposure was higher in pts with HCC vs pts with BTC (12,385 vs 5,992 ng·h/mL). Best responses were complete response in 1 pt (2%), partial response in 2 pts (4%), and stable disease (SD) in 30 pts (57%). Response rate and disease control rate were 6% and 62%, respectively.

Conclusions

Tivantinib demonstrated a manageable safety profile and was well tolerated at doses up to 360 mg BID in pts with BTC and up to 240 mg BID in pts with HCC. Only pts with HCC had increased exposure, presumably due to disease-specific hepatic impairment. Encouraging clinical activity (primarily SD) was observed in this pt population.

Disclosure

F. Chai: F Chai is an employee of ArQule, Inc., the sponsor of the studies and holds ArQule stock.

G. Abbadessa: G Abbadessa is an employee of ArQule, Inc. and owns ArQule stock options.

R. Savage: R Savage is currently an employee of ArQule and participates in the ESPP employee stock purchase plan and receives stock options as part of his compensation package as an employee of ArQule.

H. Zahir: H Zahir is an employee of Daiichi Sankyo, Inc.

Y. Chen: Y Chen is an ArQule employee and own ArQule stocks.

M. Lamar: M Lamar is an employee of ArQule, Inc.

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