1198P | A RANDOMIZED PHASE (PH) 2 STUDY WITH EXPLORATORY BIOMARKER ANALYSIS OF FICLATUZUMAB (F) A HUMANIZED HEPATOCYTE GROWTH FACTOR (HGF) INHIBITORY MAB IN COMBINATION WITH GEFITINIB (G) VERSUS G IN ASIAN PATIENTS (PTS) WITH LUNG ADENOCARCINOMA (LA)

T.S.K. Mok[1], K. Park[2], S.L. Geater[3], S. Agarwal[4], M. Han[4], M. Credi[4], K. McKee[4], N. Kuriyama[4], W. Slichenmyer[4], E.H. Tan[5]

[1]Shatin, Hong Kong/CN, [2]Seoul/KR, [3]Songkla/TH, [4]Cambridge, MA/US, [5]Singapore/SG

Background

HGF/cMet pathway activation has been implicated in EGFR TKI resistance in LA. F is an HGF IgG1 inhibitory MAb that prevents cMet receptor activation by blocking its only known ligand, HGF. This study compared FG with G in treatment naïve pts with high incidence of sensitizing EGFR mutation (SM +), and explored other biomarkers.

Methods

This was a multicenter, open-label, randomized Ph 2 Study in Asian pts with LA. Pts received either G (250 mg daily) or F (20 mg/kg IV q 2 wks) plus G (250 mg daily). Pts on G were allowed to cross over to FG upon disease progression. Primary endpoint was ORR. The secondary endpoints included PFS and correlation of biomarkers with clinical activity. Biomarker analysis included EGFR mutation status, cMet and HGF expression, EGFR and cMet gene copy number.

Results

188 pts were randomized, 94 (19M/75F) to FG or G, respectively; mean age (FG: 59, G: 60) yrs; ECOG-PS was balanced between arms. Tumor tissue samples were analyzed from 144 of 188 subjects. Table 1 shows efficacy by biomarker subset and includes results for overall population. Notable difference was seen in low cMet group, ORR (41 v 22%) and mPFS (7.3 v 2.8 m), favoring FG. The difference can be mostly attributed to the SM + /cMet low subset ORR (70 v 44%) and mPFS (11.0 v 5.5 m) favoring FG. The low cMet group may identify a subgroup in SM + that had worse outcome by G (mPFS 5.5 v 7.4 m in SM + overall) and benefited from FG treatment (11.0 m). There is also a trend in OS favoring FG in several biomarker subsets. FG demonstrated a manageable toxicity profile. FG G N PFS, m ORR,% N PFS, m ORR,% Overall Population 94 5.6 43 94 4.7 40 Biomarker Subset N PFS, m ORR,% N PFS, m ORR,% SM + 33 9.2 58 38 7.4 61 SM- 24 1.8 25 30 1.9 10 cMet Low 22 7.3 41 23 2.8 22 cMet High 34 7.4 44 44 5.5 30 SM + /cMet Low 10 11.0 70 9 5.5 44 SM-/cMet Low 9 1.3 0 13 2.3 0

Conclusions

FG was well tolerated and showed clinical activity in biomarker subsets. However, the study results did not reach statistical significance. FG appears to improve treatment outcome in a subset of pts with SM + and low cMet expression. These observations warrant further evaluation.

Disclosure

S. Agarwal: Employed by AVEO Pharmaceuticals, Inc. Involved in the design, execution, data analysis, and interpretation, of this trial.

M. Han: Employed by AVEO Pharmaceuticals, Inc. Involved in the design, execution, data analysis, and interpretation, of this trial.

K. McKee: Employed by AVEO Pharmaceuticals, Inc. Involved in the design, execution, data analysis, and interpretation, of this trial.

M. Credi: Employed by AVEO Pharmaceuticals, Inc. Involved in the design, execution, data analysis, and interpretation, of this trial.

N. Kuriyama: Employed by AVEO Pharmaceuticals, Inc. Involved in the design, execution, data analysis, and interpretation, of this trial.

W. Slichenmyer: Employed by AVEO Pharmaceuticals, Inc. Involved in the design, execution, data analysis, and interpretation, of this trial.

All other authors have declared no conflicts of interest.

Session Info: Poster, [] Poster presentation I
Day/Date: Saturday, September 29, 2012
Session Time: 1:00 PM - 2:00 PM
Room: Hall XL