9-2019

Phase 1 Trial of Fruquintinib in Patients with Advanced Solid Tumors: Results of the Dose Escalation Phase.

A Wang-Gillam

H Park

H Yeckes-Rodin

Thomas Stanton
Providence St. Joseph Health

M Kosmo

See next page for additional authors

Authors
A Wang-Gillam, H Park, H Yeckes-Rodin, Thomas Stanton, M Kosmo, S Fan, N Sauter, and M Kanie

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Background: Fruquintinib (Fruq) is a potent, highly selective, novel vascular endothelial growth factor receptor (VEGFR) -1, -2, and -3 tyrosine kinase inhibitor. In the Phase III FRESCO trial[1] that led to the drug approval in China, Fruq improved the median overall survival in patients with metastatic colorectal cancer (mCRC) in the third line or later setting when compared to placebo (9.3 vs 6.6 months); hazard ratio 0.65 (95% CI, 0.51-0.83; P < .001),

Methods: This is a Phase 1 open-label, dose escalation/dose expansion study conducted in the US (NCT03251378). The primary objectives are to evaluate the safety and tolerability of Fruq in pts with advanced solid tumors and to determine the recommended phase 2 dose (RP2D). A secondary objective is to evaluate anticancer activity. There were 2 dose cohorts: 3mg and 5 mg qd, each on a 3 weeks on, 1 week (3/1) off schedule.

Results: Fourteen pts were enrolled: 7 (6 evaluable) pts in each dose cohort. Fruq was generally well-tolerated. There was 1 dose-limiting toxicity (DLT) of grade 4 hypertension in the 3 mg cohort, and no DLTs in the 5 mg cohort. The RP2D was 5 mg qd (3/1), which is also the approved dose in China. Two other serious adverse events were reported: colon obstruction and left breast cellulitis; neither was suspected to be drug-related. All 14 pts reported AEs; the most common were vomiting (57%), nausea (50%), constipation (50%, proteinuria (50%), hypertension (50%), dysphonia (43%), anorexia (36%), and dyspepsia (36%). Ten pts were evaluable for best objective response; results were partial response 3, stable disease 6, and disease progression 1. Objective response rate was 3/14 (21.4%) and disease control rate was 9/14 (64.3%). Mean duration on study drug was 5.3 months.

Conclusion: Fruq is generally well-tolerated in heavily pretreated patients. The RP2D in US pts is 5 mg qd (3/1). The safety profile is consistent with that of other anti-angiogenic tyrosine kinase inhibitors. There is preliminary evidence of anticancer activity in pts with advanced solid tumors. The dose expansion phase of the study is ongoing. Further investigation of Fruq in pts with mCRC is planned. 1. JAMA 2018; 319:2486.