Phase 1 Study of Fisogatinib (BLU-554) in Patients (pts) with Advanced Hepatocellular Carcinoma (aHCC) Expressing FGF19: Preliminary Results from Chinese Pts in Part 3 of the Study

Category: Hepatobiliary Pancreatic-Hepatic Cancer

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Background
Emerging data have implicated the FGF19-FGFR4 signaling pathway as an oncogenic driver in HCC. Fisogatinib, a highly potent and selective FGFR4 inhibitor, was first evaluated in this global phase 1 study (NCT02508467) in aHCC pts. Parts 1 and 2 of the study demonstrated that FGFR4 inhibition was tolerable and clinically active in HCC expressing FGF19. Further investigation of fisogatinib in FGF19-positive, tyrosine kinase inhibitor (TKI) treatment-naïve pts with aHCC (part 3) is ongoing globally, and we report preliminary data from Chinese pts.

Methods
Pts with aHCC, ECOG PS 0-1, Child-Pugh Class A, FGF19 IHC-positive (staining of ≥ 1% of cells) and no prior TKI treatment were enrolled to receive fisogatinib 600 mg once daily. The primary endpoint is safety. Secondary endpoints include clinical activity by investigator assessment using RECIST v1.1, FGF19 IHC levels and pharmacokinetics evaluations.

Results
As of 4 Mar 2020, 11 pts were treated; 7 pts remained on treatment and 4 pts discontinued due to disease progression. Efficacy evaluation demonstrated an overall objective response rate of 36.4% (4/11 achieved partial response, 2 responses were confirmed) and 4 had stable disease. The disease control rate was 72.7%. Among the 4

responders, the FGF19 IHC levels were between 5% and 100% with no direct correlation to clinical response. All pts had treatment-related adverse events (TRAEs), with the most common ones being ALT increased (90.9%), diarrhea (81.8%), AST increased (72.7%) and blood bilirubin increased (63.6%); 3 (27.3%) pts had grade 3 TRAEs; no grade 4/5 TRAEs occurred. The geometric mean C_{trough} in Chinese pts was 2040 ng/mL, comparable to that in global pts.

Conclusion

Fisogatinib demonstrated a manageable side effect profile in Chinese pts that is consistent with FGFR4 pathway inhibition. Encouraging preliminary efficacy was observed in FGF19-positive, TKI treatment-naïve Chinese pts, which further validated the oncogenic role of the FGFR4 pathway and the use of FGF19 as a biomarker for patient selection in HCC. A clinical trial to evaluate fisogatinib in combination with CS1001 (anti-PD-L1) in aHCC is ongoing.