Phase (Ph) 1/2 Study of Sitravatinib (Sitra) Alone or With Tislelizumab (TIS) in Advanced Hepatocellular Carcinoma (HCC) and Gastric/Gastroesophageal Junction Cancer (GC/GEJC)

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Background: Sitra, a spectrum-selective tyrosine kinase inhibitor, may enhance the efficacy of programmed cell death protein 1 (PD-1) inhibition. TIS, an anti-PD-1 antibody, has demonstrated efficacy in multiple advanced solid tumors. SAFFRON-104 is a multi-cohort Ph 1/2 study investigating sitra +/- TIS in patients (pts) with advanced HCC or GC/GEJC (NCT03941873).

Methods: Eligible pts had histologically/cytologically confirmed unresectable locally advanced or metastatic HCC or GC/GEJC. Pts enrolled in Ph 1 (dose escalation) received free base sitra (80 or 120 mg orally once daily) alone or combined with TIS (200 mg IV once every 3 weeks); Ph 1 determined the recommended Ph 2 dose (RP2D). Ph 2 evaluated sitra alone in pts with HCC who were naïve or refractory/resistant (R/R) to anti-PD-(L)1 therapy and sitra + TIS in pts with anti-PD-1/programmed death-ligand 1 (PD-L1)-naïve HCC, anti-PD-(L)1 R/R HCC, and anti-PD-(L)1-naïve GC/GEJC. Primary endpoints were safety/tolerability (Ph 1) and objective response rate (ORR) by RECIST v1.1 (Ph 2). Secondary endpoints included disease control rate (DCR), duration of response (DoR), and progression-free survival (PFS).

Results: As of Jan 4, 2023, 111 pts were enrolled, of whom 102 were efficacy-evaluable (median study follow-up 9.1 months [range 0.7-34.0]). The RP2D of sitra determined in Ph 1 was 120 mg orally once daily. In pts receiving sitra +/- TIS, respectively, any-grade treatment-related adverse events (TRAEs) were reported in 74 (89.2%) and 24 (100%); ≥grade 3 TRAEs in 37 (44.6%) and 13 (54.2%); and serious TRAEs in 19 (22.9%) and 6 (25.0%). TRAEs leading to treatment discontinuation were reported in 10 (12.0%) pts and 1 (4.2%) pt receiving sitra +/- TIS, respectively. Pooled efficacy data from Ph 1 and 2 by indication are shown in the **Table**.

Conclusions: Sitra +/- TIS was generally well tolerated and showed preliminary antitumor activity in pts with advanced HCC and GC/GEJC.

	HCC			**GC/GEJC[a]**
Treatment	**Sitra**	**Sitra + TIS**		**Sitra + TIS**
Prior anti-PD-(L)1 treatment	**Naïve or R/R (n=20)**	**Naïve (n=26)**	**R/R (n=21)**	**Naïve (n=31)**
ORR, n (%)	5 (25.0)	3 (11.5)	2 (9.5)	5 (16.1)
DCR, n (%)	18 (90.0)	22 (84.6)	17 (81.0)	22 (71.0)
Median DoR, mo (95% CI)	7.7 (2.8, NE)	5.7 (4.1, NE)	NR (5.4, NE)	5.5 (2.7, NE)
Median PFS, mo (95% CI)	6.8 (4.0, 7.4)	6.8 (2.8, 8.3)	4.2 (2.7, 6.8)	3.6 (2.8, 4.7)

Efficacy analysis set. [a]Four patients with GC/GEJC enrolled in Ph 1 were not included in the efficacy or safety analysis by indication because they were either anti-PD-(L)1 R/R or received sitra monotherapy.
CI, confidence interval; mo, months; NE, not estimable; NR, not reached.