- Preliminary efficacy was evaluated according to RECIST 1.1. Overall, confirmed partial response (PR) was obtained in 1 UC patient with H&E receiving 10 mg QD. And stable disease (SD) was observed in 1 UC patient with H&E, 1 UC patient with NG, and 1 UC patient with ileal tube cancer (Figure 2a).

- Safety

- A Phase I study of Safety, Pharmacokinetics, and Pharmacodynamics of SCR-6920, a Protein Arginine Methyltransferase 5 (PRMT5) Inhibitor, in Patients with Advanced Malignant Tumors

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STUDY DESIGN

- Patients with advanced malignant tumors were enrolled in this first-in-human, multicenter, open-label Phase I study (NCT03753280). SCR-6920 was administered orally, once daily (QD) on a 21-day cycle. The dose was escalated in a 3+3 design. A total of 27 patients were enrolled (data cut-off date: 30 June 2022). Study treatment was continued until disease progression, patient withdrawal, or the end of the study (Figure 1).

- The Phase 1 study was conducted at four centers (Beijing, Tianjin, Shanghai, and Xiamen) in China.

- A Bayesian Optimal (BayOpt) design was used to guide dose escalation with a starting dose level of 10 mg QD.

- The primary objective was to evaluate the safety and tolerability and to determine the maximum tolerated dose (MTD) and the recommended phase II dose (RP2D) of SCR-6920.

RESULTS

- A total of 25 patients were included in the study, and 22 patients were assessable for efficacy. Among them, 21 patients were assessable for safety and tolerability. The median age (range) was 62 (42-71) years. Sex, n (%): female, 11 (50.0%); male, 14 (60.0%).

- The tumor types included gastric cancer (5), breast cancer (4), lung cancer (4), colorectal cancer (4), cervical cancer (3), small cell lung cancer (2), and other malignancies (10). The median number of prior treatment lines (range) was 1 (0-4) for gastric cancer, 1 (0-4) for breast cancer, 1 (0-3) for lung cancer, 2 (0-4) for colorectal cancer, 1 (0-3) for cervical cancer, and 1 (0-3) for other malignancies.

- The median duration of response (DOR) was 9.4 weeks (range: 2.2-30.7 weeks).

- The median time to progression (TTP) was 10.1 weeks (range: 0.5-23.3 weeks).

- The median overall survival (OS) was 29.4 weeks (range: 0.5-102.3 weeks).

- SCR-6920 was well tolerated at all dose levels. The most common AE was Grades 1-2 diarrhea (16 patients, 64.0%), followed by Grade 1-2 nausea (9 patients, 36.0%), Grade 1-2 vomiting (7 patients, 28.0%), and Grade 1-2 fatigue (6 patients, 24.0%). Other AEs included Grade 1-2 proteinuria, Grade 1-2 arthralgia, and Grade 1-2 dyspepsia.

- AEs occurred in 19 patients (76.0%), with 5 (20.0%) patients having Grade 3 or 4 AEs, including Grade 3 fatigue (2 patients, 8.0%), Grade 3 proteinuria (2 patients, 8.0%), and Grade 4 proteinuria (1 patient, 4.0%). There were no dose-limiting toxicities (DLTs), and no patient discontinued due to treatment-related toxicity.

- Steady-state plasma exposure (AUC) increased with increasing dose levels (Figure 5).

- SCR-6920 was well tolerated at all dose levels and showed manageable tolerability at the RP2D of 40 mg QD.

- SCR-6920 showed clear anti-tumor activity in patients with advanced malignant tumors, with a median DOR of 9.4 weeks and a median TTP of 10.1 weeks. SCR-6920 was recommended for Phase II study at 40 mg QD, based on its manageable safety profile and tolerability at this dose level.

CONCLUSIONS

- SCR-6920 had a manageable safety profile and further advancements are ongoing to determine the RP2D.

References