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527P - Phase 1 study of the novel prodrug MIV-818 in patients with hepatocellular carcinoma (HCC), intrahepatic cholangio-carcinoma (iCCA) or liver metastases (LM)

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Background: MIV-818 is an orally administered troxacitabine-based nucleotide prodrug currently undergoing phase 1 clinical trial (NCT03781934). It is rapidly metabolized by human hepatocytes, directing high levels of the chain-terminating nucleotide tri-phosphate to the liver, while minimizing exposure to other organs.

Methods: Patients (pts), ≥18 years, ECOG performance status < 1, adequate organ function, with advanced inoperable HCC, iCCA or LM from solid tumours of gastrointestinal origin were enrolled. MIV-818 as a single agent was administered as an inter-patient dose escalation 3+3 cohort design. The primary objective is to assess safety and tolerability. A key secondary objective was to evaluate the overall response rate based on RECIST v1.1. As exploratory objectives, on-treatment liver biopsies were collected to assess the pharmacokinetics and the pharmacodynamic effects of MIV-818.

Results: Nine evaluable pts (6M; 3F), median age = 64 years (range: 47-74) with HCC (5), mixed HCC/iCCA (1) iCCA (1) or LM (2) from GI tract solid tumours, previously treated with median 2 (1-7) lines of therapy, were included. Starting dose was 40 mg for 5 days in 21-day cycles. The most common treatment emergent AEs were those in the haematological system; raised LFTs and pruritus were also commonly reported. Out of 9 pts, one pt experienced a DLT (Maculopapular rash grade 3) during the first cycle of treatment. The longest duration of treatment was 9 cycles; seen in 1 pt. Tumour biopsies showed evidence of selective, drug-induced, DNA damage, measured as phosphorylation of histone H2AX, in tumour tissue with minimal or no impact of MIV-818 observed in healthy liver tissue.

Conclusions: MIV-818 had an acceptable safety and tolerability profile, with haematological suppression being the most common AE. Biomarker data of liver biopsies demonstrated a selective effect of MIV-818 on cancer cells. The study will now evaluate MIV-818 in combination with other agents in HCC patients.