Background: LioCyx-M is an immunotherapeutic product based on autologous T cells transiently modified with in vitro transcribed mRNA encoding HBV-specific T-cell receptors (TCR). We have previously shown, in a compassionate setting, the ability of LioCyx-M cells to recognize and lyse hepatocellular carcinoma (HCC) expressing HBV antigens derived from HBV-DNA integration in patients with HCC recurrence post-liver transplant. Here, we report our phase I study aimed to determine the feasibility, safety and preliminary efficacy of LioCyx-M in recurrent HBV-related HCC post-liver transplantation.

Methods: Eligible patients with HBsAg-positive recurrent HCC as well as HLA-matched to selected TCRs were enrolled in this study. All patients underwent leukapheresis prior to treatment cycle, patients received 4 escalating doses of $1 \times 10^4$ cells/kg BW (n=1) and $1 \times 10^5$ cells/kg BW administrated every 7 days for 4 weeks. The median overall survival was 14 months (range: 4 - 22 months). Only fever syndrome- and neurotoxicity-like AEs were observed. Out of 6 patients evaluable for tumor response, the median time to progression was at 1.3 months (range: 1.2 - 1.6 months). Six patients were enrolled, with a median age of 35.5 years.

Results: Six patients were enrolled, with a median age of 35.5 years (range: 28 - 47). These patients received a median number of 6.5 doses of LioCyx-M therapy (range: 4 - 12). Only fever was observed as treatment-related AEs. Grade 1 fever was observed at dose levels of $1 \times 10^4$ cells/kg BW (n=1) and $1 \times 10^5$ cells/kg BW (n=3) respectively. No cytokine release syndrome- and neurotoxicity-like AEs were observed. Out of 4 patients evaluable for tumor response, the median of tumor progression was at 1.3 months (range: 1.2 - 1.6 months). The median overall survival was 14 months (range: 4 - 22 months). At data cutoff (30 April 2020), one patient was still alive and 5 were deceased.

Conclusions: Our data showed that multiple infusions of LioCyx-M are well tolerated at all dose levels administrated in recurrent HCC post liver transplantation, with no adverse effect to the transplanted liver. This calls for further assessment in a Phase 2 study.

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Trial Registration: NCT02719782

Ethics Approval: The study was approved by Sun Yat-Sen Third Affiliated Hospital’s Ethics Board, approval number [2015]2-157.