REFERENCE

1. Tan AT, Yang N, Lee Krishnamoorthy T, *et al*. Use of Expression Profiles of HBV-DNA Integrated Into Genomes of Hepatocellular Carcinoma Cells to Select T Cells for Immunotherapy. *Gastroenterology* 2019;**156**(6):1862–1876.e9.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0272

273 PHASE I STUDY OF LIOCYX-M, AUTOLOGOUS HEPATITIS B VIRUS (HBV)-SPECIFIC T CELL RECEPTOR (TCR) T-CELLS, IN RECURRENT HBV-RELATED HEPATOCELLULAR CARCINOMA (HCC) POST-LIVER TRANSPLANTATION

[1]Wenjie Chen, [1]Jintao Cheng*, [1]Xiaofang Zheng, [1]Fan Yang, [2]Royce Fam, [3]Sarene Koh, [3]Lu-En Wai, [2]Tingting Wang, [4]Antonio Bertoletti, [1]Qi Zhang. [1]3rd Aff Hospital, Sun Yat-Sen University, Guangzhou, China; [2]Lion TCR Pte Ltd, Singapore, Singapore; [3]Lion TCR Pte Ltd, A*STAR, Singapore, Singapore; [4]Lion TCR Pte Ltd,Duke-NUS Medical School, Singapore, Singapore

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.[1] 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 and peripheral blood mononuclear cells (PBMC) were collected for LioCyx-M manufacturing. During the 1st treatment cycle, patients received 4 escalating doses of 1×10^4 cells/kg, 1×10^5 cells/kg, 1×10^6 cells/kg, 5×10^6 cells/kg bodyweight (BW) intravenously every 7 days. Adverse events were evaluated by Common Terminology Criteria for Adverse Events Version 4.0. In the second treatment cycle, one infusion of LioCyx-M at dose of $1–5 \times 10^6$ cells/kg BW was intravenously administrated every 7 days for 4 weeks. The anti-tumour efficacy of LioCyx-M was evaluated per RECIST 1.1 criteria and survival was followed-up during the study.

Results Six patients were enrolled, with a median age of 35.5 (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 1×10^4 cells/kg BW (n=1) and $1–5 \times 10^6$ 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 time to 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.

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

REFERENCE

1. Tan AT, Yang N, Lee Krishnamoorthy T, *et al*. Use of Expression Profiles of HBV-DNA Integrated Into Genomes of Hepatocellular Carcinoma Cells to Select T Cells for Immunotherapy. *Gastroenterology* 2019;**156**(6):1862–1876.e9.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0273

274 TUMORAL AND PERIPHERAL IMMUNOPHENOTYPE OF REFRACTORY VS RELAPSE TO PD-(L)1 BLOCKADE IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER

[1]Maria Ascierto*, [2]Matthew Hellmann, [1]Nathan Standifer, [1]Song Wu, [1]Han Si, [1]Chris Morehouse, [1]Marlon Rebelatto, [1]Shaad Abdullah, [1]Rajiv Raja, [1]Jean-Charles Soria, [1]Caroline Germa, [1]Carl Barrett. [1]Astrazeneca, Gaithersburg, MD, USA; [2]MSK, New York, NY, USA

Background Despite the encouraging successes of immune checkpoint inhibitors, many patients do not benefit and are either refractory or relapse. The mechanisms of refractory or relapsed disease following PD-(L)1 blockade are largely unknown. To identify characteristics associated with refractory or relapsed disease we explored the immune and genomic landscape of samples derived from NSCLC patients who previously received PD-(L)1 blockade and had blood and fresh tumor biopsies collected at the time of progression.

Methods Patient response categories were defined prospectively; 'refractory' defined as progression within 16 weeks of initiating PD-(L)1 and 'relapse' defined as initial clinical benefit (CR, PR, SD) followed by progression. RNAseq (n=52) and PD-L1 IHC (n=22) were performed on tumor tissue. Immune profiling of whole blood was assessed using flow cytometry or Biomark HD (Fluidigm) gene expression panel (n=54 and n=62, respectively). Differential gene expression was defined as unadjusted p<0.05 and fold-difference >1.5. Pathways analysis was conducted by David tool. Patient samples were collected during screening for clinical trial of second line immunotherapy. Written informed consent was obtained from the patients for publication of this abstract.

Results In patients with NSCLC previously treated with PD-(L)1 blockade, tumors of relapsed patients were characterized by increased expression of genes associated with interferon signaling (e.g. CXCL9, SPIC, IFNg), immune suppression (e.g. ARG1, TGFB), immune exhaustion (e.g. ADORA2A), and increased PD-L1 expression (by gene expression and IHC). Refractory disease was associated with increased cadherin signaling and calcium-dependent-cell-adhesion gene expression pathways. In the periphery, reduced quantities of B cells and activated (HLA-DR+ or CD38+) or proliferating (Ki67+) CD8+ T cells were observed in refractory patients.

Conclusions The tumor and peripheral compartments of patients with NSCLC previously treated with PD-(L)1 blockade differ based on prior response. Relapsed patients tend to have signals of sturdy immune activation and chronic inflammation thus ultimately leading to immune exhaustion. These results may help inform rational therapeutic strategies to overcome resistance to PD-(L)1 blockade in NSCLC.

Ethics Approval Research on human samples here analyzed have been performed in accordance with the Declaration of Helsinki.

Consent Written informed consent was obtained from the patient for publication of this abstract.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0274