ELSEVIER

Blood 142 (2023) 4837–4838

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Ksd-101 in Patients with EBV-Associated Hematologic Neoplasms: Results from an Ongoing Phase I Clinical Study

Chunrui Li[1,2], *Di Wang*[3], *Atsuhiko Hasegawa, DVM,PhD*[4], *Huining Liu, MDPhD*[5], *Ning An*[6], *Yuhan Bao*[6], *Meijuan Huang, MD*[7], *Yi Xiao, MDPhD*[8], *Donghua Zhang*[2], *Miao Zheng, MDPhD*[9], *Wei Huang, MDPhD*[9], *Lijun Jiang, MDPhD*[9]

[1] Institute of Hematolog;Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, CHN
[2] Department of Hematology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
[3] Institute of Hematolog; Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
[4] Tumor Cell Biology, Clinical Research Institute, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan
[5] KOUSAI Bio Co.,Ltd, Shanghai, China
[6] Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Wu Han, China
[7] Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
[8] Tongji Hospital affiliated to Tongji Medical College of Huazhong University of Science & Technology, Wuhan, China
[9] Department of Hematology, Tongji Hospital of Tongji Medical College, Huazhong Un, Wuhan, China

Background: The Epstein-Barr Virus (EBV), which has been confirmed by WHO as the first human tumor-associated virus, is a lifelong carrier once infected. EBV-associated Hematologic Neoplasms seriously threats human health, with rapid disease progression, poor prognosis, easy to relapse, and high mortality rate. KSD-101 is a First-in-class autologous dendritic cell (DC) vaccine which is developed to control EBV-associated hematological diseases. Autologous DCs were loaded with the EBV-transformed B-LCL (B-Lymphoblastoid Cell Line) lysates which contains a broad-spectrum EBV antigen to prepare KSD-101 for the treatment of EBV-associated diseases.

Methods: In this study, patients (pts) with EBV-associated Hematologic Neoplasms who fail to respond to or relapse after conventional treatment will be recruited and undergo leukapheresis to collect autologous peripheral blood mononuclear cell (PBMC). The enriched monocytes will be induced to differentiate into DCs and prepared as KSD-101 after loading with EBV-transformed B-LCL. Pts will undergo monotherapy with KSD-101, without the need for pre-treatment of lymphodepletion or prophylactic medication. Administration route of KSD-101 is subcutaneous injection, once every 2 weeks for 3-5 vaccinations in total. The study used a 3+3 dose-escalation design. Safety assessment is conducted according to NCI-CTCAE 5.0 grading criteria. The primary objective is to assess the tolerability and safety of KSD-101 in the treatment of EBV-associated Hematologic Neoplasms, explore the dose-limiting toxicities (DLT) and the maximum tolerated dose (MTD). The secondary objective is to explore the clinical efficacy and immune responses of KSD-101 in the patients with EBV-associated Hematologic Neoplasms.

Results: As of July 2023, 9pts were enrolled in the study and 8 pts DC vaccine preparations were completed. Three pts were injected 5.0×10^6 cells/dose without exploring any DLT. The first two pts in the second dose level were injected 7.5×10^6 cells/dose. However, the third pt in second dose level was injected 5.0×10^6 cells/dose due to insufficient apheresis collection. Based on the safety and preliminary efficacy data, we decided not to proceed with dose-escalation to the third dose group. In the expansion phase, all pts were injected with a dose of 5.0×10^6 cells. Currently observed KSD-101-related toxicities were pyrexia (grade ≤ 2), injection site reactions (grade 1), and lymphadenopathy (grade 1). In all the pts who were injected, neither DLT nor MTD were explored. Based on the comprehensive considerations of safety, efficacy and easibility, we propose that the most appropriate dose is 5.0×10^6 cells.

Of all pts enrolled, one was excluded due to hemophagocytic lymphohistiocytosis (HLH), among whom 4 pts completed the 12-week follow-up after the first injection for clinical and laboratory assessments. The results showed an overall response rate (ORR):100%, complete response (CR):100%, including 1 case of AITL (EBV infected T, B, NK),1case of CAEBV (EBV infected T, NK),2cases of NK-T cell lymphoma (1 EBV infected B, NK, and the other EBV infected NK). After vaccinations, the total

number of lymphocytes of these four pts increased by 1.5 to3.4 times, including 1.6 to 4.2 times of T cells, 2.1 to 6.5 times of activated T cells ($CD3^+$ HLA^-DR^+), 1.4 to 5.0 times of $CD8^+$ T cells, 1.2 to 3.7 times of $CD4^+$ T cells, 1.7 to 2.0 times of NK cells, and 1.2 to 32.4 times of B cells; meanwhile, the proportion of EBV-specific CTLs increased significantly (ranging from a 2.51% to 4.16% increase), and the proportion of Tregs significantly decreased compared with the baseline (ranging from a 32.49% to 73.81% reduction).
Conclusions:Our current study shows that KSD-101 has excellent safety and good preliminary efficacy against EBV-associated Hematologic Neoplasms with efficient induction of immune responses. The results indicate that KSD-101 is a promising therapeutic reagent for the treatment of EBV-associated Hematologic Neoplasms. Larger prospective studies and longer follow-up time is needed to be conducted.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-182556