Abstract: P1439

Title: DENDRITIC CELL-BASED VACCINES (KSD-101) AGAINST EBV-ASSOCIATED HEMATOLOGIC NEOPLASMS: RESULTS FROM AN ONGOING PHASE I CLINICAL STUDY

Abstract Type: Poster Presentation

Topic: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

The Epstein–Barr Virus (EBV) infects more than 95% of people in the world. EBV is confirmed by WHO as the first human tumor-associated virus, EBV-associated hematologic neoplasms seriously threats human health. KSD-101 is a First-in-class autologous dendritic cell (DC) vaccine against EBV-associated hematologic neoplasms loaded with the EBV-related antigen.

Aims:

Our ongoing phase I study is to evaluate the safety and efficacy of KSD-101 (NCT05635591). The primary endpoint is to evaluate tolerability, safety, dose-limiting toxicities (DLT) and the maximum tolerated dose (MTD). The secondary endpoint is to explore the clinical efficacy and immune response.

Methods:

Patients (pts) with EBV-associated hematologic neoplasms who failed to respond to or relapsed after conventional treatment will be recruited. Pts will undergo monotherapy with KSD-101 by subcutaneous injection, once every 2 weeks for 3-5 vaccinations, without the need for pre-treatment of lymphodepletion or prophylactic medication. The study used a 3+3 dose-escalation design.

Results:

AS of October 30, 2023, 9 pts received KSD-101 at least 3 doses. In the escalation phase, 3 pts received 5.0 × 106 cells/dose and 2 pts received 7.5 × 106 cells/dose. Based on the safety, preliminary efficacy, and feasibility assessment, we decided to cancel the third dose group and apply 5.0 × 106 cells/dose to the expansion phase. In all pts, neither DLT nor MTD were explored. Vaccinations were well tolerated. Pts experienced KSD-101-related toxicities were fever (grade ≤ 2), injection site reactions (grade 1), lymphadenectasis (grade 1) and lymphocyte count increased (grade 1). In 5 efficacy-evaluable pts (1 was excluded due to early disease recurrence, 2 didn't reach the time for efficacy evaluation and 1 was not included for other reasons), the ORR was 100% and the CR rate was 100%, including 1 case of AITL (EBV infected T, B, NK), 1 case of CAEBV (EBV infected T, NK), 2 cases of NK-T cell lymphoma (one EBV infected B, NK, one EBV infected NK) and 1 case of DLBCL (peripheral T-cell lymphoma transformation, EBV infected B, NK). After vaccinations, we found that the peak proportion of EBV-specific T cells in CD3+CD8+ T cells (average, 2.47%) was significantly increased ($p < 0.05$) compared to baseline (average, 0.30%) and the peak number of immune cells also increased, such as B cells ($p < 0.05$, average increased to 27.51-fold), NK cells ($p < 0.01$, average increased to 1.68-fold) and CD8+ T cells ($p < 0.05$, average increased to 2.38-fold). We also found that the valley number of T-regs significantly reduced ($p < 0.001$, average reduced to 53.05%).

Summary/Conclusion:

AS of now, KSD-101 has been demonstrated good safety and efficacy and could activate immune system. Our study indicates that the KSD-101 is a promising therapeutic reagent for the treatment of EBV-associated hematologic neoplasms. Larger prospective studies and longer follow-up time are needed to be conducted.

Keywords: Dendritic cell vaccine, Clinical trial, EBV, Hematological malignancy