Pre-Clinical Development

Framework of Pre-Clinical Development

Multi-HLA binding peptide selection with AI-based prediction

Selection of immunogenic Multi-HLA reactive peptides using patients PBMC

HSP70 and GPC3, complementarily highly expressed in various cancers

Complementary expression of HSP70 and GPC3 in area basis

Detection of immunogenic HLA-A24
dwell with AI-based prediction

One-HLA binding peptide selection with AI-based prediction

Clinical Progression

A phase I study of combination immunotherapy with HSP70 derived peptide, GPC3 derived peptide, IMP321 and Hiltonol for patients with advanced or metastatic solid cancer

Vaccination schedule

Dosage (mg) Level Peptides Adjunctives

Enrolled patients: 17, Period (incorporation): 2016/1 - 2017/9

Results - Endpoints

1. Safety - The incidence of adverse events

2.1 Antigen-peptide reactive immune response

2.2 Biomarker response in PBMC

2.3 Anti-tumor effects

YNP01 Study

AI-designed dual peptide vaccine for HSP70/Glycan-3 plus Poly ICLC showed a markedly effective induction of antigen-specific CTLs with disease stabilization in last patients with GI cancers.

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Background: Recent advances in cancer immunology, such as the discovery of immune checkpoint inhibitors (ICIs), have validated T cells as potential key players for effective cancer treatment. However, ICIs showed limited anti-cancer activity against GI cancers because ICIs are supposed to be inactive against relatively "cold" GI tumors. Peptide vaccines with appropriate adjuvants are the most promising strategy to induce tumor-reactive T cells and may turn "cold" tumor into "hot" tumor. In previous studies, we have identified that HSP70 and GPC3 as the appropriate cancer antigens for peptide vaccine therapy in GI cancer (Yoshida S. et al., Anticancer Res., 2009, 29:539-544). We have also revealed that combination of soluble LAG-3 (LAG-3g), a novel DC activator, and Poly ILC exhibited synergistic robust adjuvant effects in mice pre-clinical models (Kano Y. et al., Cancer Science, 2016, 107:398-406).

In this study we identified the HSP70 or GPC3 peptides that have higher binding affinity in each of HLA-A*24:02, 02:01 and 02:06 by using a AI-based peptide prediction system developned by NEC Corp. Based on these studies, we have conducted First time in human Phase 1 study of HSP70/GPC3 dual peptide vaccine plus combinations of LAG-3g (IMP321(efilagimab), immuone) and Poly ICLC (Hiltonol, Oncovir). We have also documented that this "danger signal" mimicking viral infection activates antigen-presenting cells, and activates APCs through this "danger signal" mimicking viral infection.

Results: Seventeen HLA-A*2402, 0201, and 0206-matched pts (esophagus(E) 5; colon(CRC) 6; liver(HCC) 4; pancreas 1; stomach 1) were treated in this study. No severe adverse effects related to the treatment were encountered. Peptide-specific CTL induction to HSP70 and GPC3 was observed in 16 and 17 pts, respectively. In patients receiving Level 3 dosage, the population of TIM3+ cells in CD4+ T cells was decreased significantly (p = 0.012), and MDSC showed trend to decrease (p = 0.131) after 1 course of treatment. OS rates in CRC, HCC, and EC were 83%, 75%, and 60% at 6M, and 50%, 75% and 0% at 12M, respectively. Low expression of PDL1 on CD4+ T cells (p = 0.02) and low proportion of Treg Fraction II (p = 0.03) in the PBMC were the significant favorable biomarker for OS.

Conclusion: The combination cancer vaccine therapy using HLA restricted HSP70/GPC3 peptides with LAG-3g and Poly ICLC adjuvants was safe and effective for rapid induction of CTL response against HSP70/GPC3.

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