Background AST-021p, which is derived from HLA class II binding epitopes of human HSP90 protein, is an investigational therapeutic cancer vaccine for the malignant neoplasms. AST-021p is designed to demonstrate the immunologic efficacy by activating antigen-specific CD4+ Th1 cell in humans. Due to their ability to link the innate with the adaptive immune response, Toll-like receptor (TLR) agonists are highly promising as adjuvants in vaccines against life-threatening and complex diseases such as cancer, AIDS and malaria. In this study, AST-021p was investigated to evaluate the immunogenicity and tumor growth inhibitory effect under the condition of combining with various immune adjuvants derived from TLR agonists, using in-vivo model.

Methods Three different agonists of TLR (TLR-4, TLR-2/3, TLR-7/8) were assigned to investigate the immunogenicity in each group (4 FVB mice/group, total 4 groups). AST-021p was intradermally injected 3 times with different TLR-agonists and the immunogenicity was assessed from mouse splenocyte by HSP90-specific IFN-γ ELISpot method. We also examined the efficacy of AST-021p and selected TLR-agonist in MMTVNeu Tg mice (4 mice/group, conducted twice and A total 8 mice was assigned to each group). The combination of AST-021p and TLR-2/3 agonist (AST-021p plus TLR-2/3 agonist) was injected 3 times every 10 days to mice followed by inoculated mouse mammary cancer cell line. The tumor volume change and immunogenicity were evaluated.

Results The most effective TLR-agonist as a potent immune adjuvant was a TLR-2/3 agonist (L-pampoTM, supplied by CHA Vaccine Institute). In MMTV-Neu transgenic mice, AST-021p (100 μg) plus TLR-2/3 agonist significantly enhanced immunogenicity by increasing up to 130±10 HSP-90 epitope specific T cells per 1x10^5 splenocytes (P<0.001). AST-021p plus TLR-2/3 agonist also showed higher tumor growth inhibitory effect (170±108 mm^3) on post-implantation 35th day by suppressing mouse mammary cancer cell line (5x10^5)-derived tumor growth, compared with a TLR-2/3 agonist alone (1031±450 mm^3).

Conclusions Combination regimen of AST-021p and TLR-2/3 agonist (as immune adjuvant) demonstrated significant immunogenicity and tumor prevention effect in in-vivo study. These data supported the clinical study of AST-021p combined with TLR-2/3 agonist as active immune adjuvant in certain tumor types, and phase 1/2 clinical program would be expected to be initiated.

Acknowledgements Not applicable

Trial Registration Not applicable

REFERENCES

Ethics Approval All experimental procedures involving mice were performed with the guidance protocols approved by the Institutional Animal Care and Use Committee of Korea University (IACUC, Approval number: KOREA-2019-129)

Consent It is not an abstract containing sensitive or identifiable information.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.860