THE ANTI-TUMOR ACTIVITY OF HSP-90 THERAPEUTIC CANCER VACCINE (AST-021p) COMBINE WITH TLR2/3 AGONIST IN A MMTV-NEU TRANSGENIC MODEL

1Jinho Kang, 2Eunkyo Joung, 3Hunwoo Shin, 4Byung chool Ahn, 5Eunjung Jung, 6Hun Jung*, 1Kyong Hwa Park.

1Korea University College of Medicine, Seoul, Korea, Republic of; 2Aston Sci. Inc, Seoul, Korea, Republic of; 3Aston Sci. Inc., Seoul, Korea, Republic of; 4CHA Vaccine Institute, Seoul, Korea, Republic of

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 MMTV-neu 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 1x10⁵ splenocytes (P<0.001). AST-021p plus TLR-2/3 agonist also showed higher tumor growth inhibitory effect (170±108 mm³) on post-implantation 35th day by suppressing mouse mammary cancer cell line (5x10⁵)-derived tumor growth, compared with a TLR-2/3 agonist alone (1031±450 mm³).

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