776 THE ANTI-TUMOR ACTIVITY OF HER-2/NEU ICD THERAPEUTIC CANCER VACCINE (AST-301, PNGVL3-HICD) IN HER2-EXPRESSED GASTRIC CANCER XENOGRAFT MODEL

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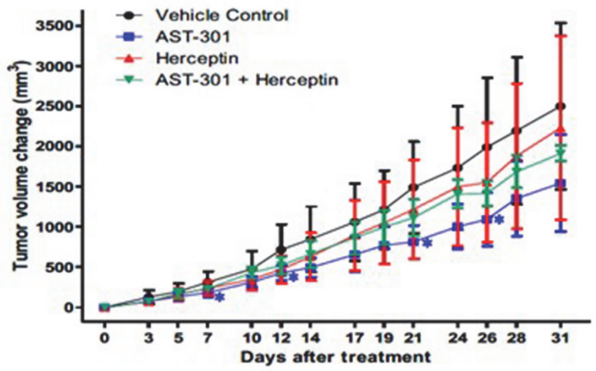
Background The HER-2/neu, potent oncogenic protein, has several characteristics that make it a good antigen to serve as the model for developing pDNA-based tumor vaccine strategies.[1–3] The observation that immunity co-exists with antigen-positive cancer cells indicates that HER-2 is immunogenic. AST-301 (pNGVL3-hICD) is a plasmid DNA-based therapeutic cancer vaccine encoding HER2 ICD sequence. The clinical efficacy and safety of AST-301 were already proven in HER2-positive breast cancer population, and long-term immunogenicity and survival were demonstrated well via phase 1 study (PN 109, NCT00436254) In this in-vivo study, AST-301 was investigated to evaluate the efficacy in HER2/neu-expressed gastric cancer xenograft model.

Methods A HER2-expressed gastric cancer xenograft model was established with NCI-N87 cell line inoculation in athymic-nude mice. Treatment groups were assigned as AST-301 alone (AST-301, 0.1 mg/head, i.d.), Trastuzumab (TZM, 20 mg/kg, i.p.) or AST-301 combining with Trastuzumab (AST-301+TZM) respectively. To evaluate tumor protective effect of drugs, mice were immunized 3 times in every week. Immunization of AST-301 or AST-301+TZM was completed, followed by tumor cell line inoculation. In another study to verify the anti-tumor effect of them, the administration of drugs was started when the tumor volumes reached approximately 150 mm^3. AST-301 was immunized 3 times in every week to post-implantation 32nd day and TZM was injected 5 times per week. The tumor volumes were estimated and the percentage of tumor growth inhibition was calculated.

Results In our two in vivo efficacy studies, there was no significant specific safety issue in all groups. Tumor protective effect was observed in AST-301 group (1506.7±1603.0 mm^3) compared with control group (GM-CSF, 1266.3±862.5 mm^3) as an immune adjuvant (figure 1). However, AST-301+TZM group (1533.0±1186.3 mm^3) did not show the tumor protective effect. The groups of AST-301 and AST-301+TZM were significantly higher to the anti-tumor activity than control group, and AST-301 was more effective than AST-301+TZM or TZM alone. On day 33 (32 days after starting treatment), tumor growth inhibition rate were 38.3 % (2503.4±1034.6 mm^3), 10.9 % (1545.0±599.9 mm^3) and 23.6 % (1912.9 ±97.1 mm^3) in groups of AST-301, TZM and AST-301 +TZM compared with control group, respectively.

Conclusions Tumor protective and tumor therapeutic effect of AST-301 were demonstrated well in various doses and regimens on HER2/neu positive gastric cancer xenograft model. These data would be supporting a proof of concept (PoC) clinical study of HER-2/neu ICD therapeutic cancer vaccine in certain type of HER2/neu-expressed gastric cancer patient.



Abstract 776 Figure 1 Tumor protective and tumor therapeutic effect of AST-301 on HER2/neu positive gastric cancer xenograft model

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Ethics Approval This experiment was conducted ethically with the approval of the Institutional Animal Care and Use Committee (KBIO-IACUC-2021-038) in the Osong Medical Innovation Foundation Experimental Animal Center.
Consent N/A

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