Background AST-301 (pNGVL3-hICD) is a plasmid DNA-based cancer vaccine encoding HER2-ICD that is not only a potent oncogenic protein but also immunogenic antigen in human cancer. The clinical efficacy and safety of AST-301, including long-term immunogenicity and survival, were demonstrated in a HER2-positive breast cancer population in a phase 1 study completed (PN109, NCT00436254). In this study, we did comparison of the antitumor effect of a combination regimen of AST-301 and HER2 ADC in athymic (immunodeficient) and CD34+ humanized models using human gastric cancer cell line.

Methods NCI-N87 cells were mixed with the same amount of matrigel to formulation tumors in mice. CD34+ humanized (n=4/group) and Athymic BALB/c nude (n=7/group) mouse were assigned. When the tumor size were reached to 100–200 mm³, study drug regimen was administrated. AST-301 (100 µg/animal, intradermal injection, mixed with rhuGM-CSF as an immune adjuvant) was immunized once a week to a total of fourth. LCB01 (IV injection) was administered with a single dosing.

Results In CD34+ humanized mouse model, a combination regimen of AST-301 and LCB01 (low does) showed better anti-tumor efficacy than LCB01 (high does) alone (TGI rate at Day 22, 64% vs 39%), and even AST-301 mono-treatment showed better anti-tumor efficacy than LCB01 (low does) alone (TGI rate at Day 22, 32% vs 24%). Whereas, in athymic BALB/c nude mouse model, AST-301 and LCB01 (low does) did not show better anti-tumor efficacy than LCB01 (high does) alone (TGI rate at day 25, 52% vs 69%).

Immune cell changes was profiled by FACS analysis in splenocytes and tumor cells of mice. In the CD34+ humanized mouse model, cytotoxic T cell was relatively increased in tumor site by the combination regimen of AST-301 with LCB01 and LCB01 (low does) alone. Also, cytotoxic T cells was increased in splenocyte by AST-301 mono-treatment and LCB01 (low does) alone.

Conclusions Given that clear antitumor effect of AST-301-based regimen was observed in CD34+ humanized mouse model than athymic BALB/c nude mouse model, it is proven that the presence of T cells is very crucial in pharmacological efficacy of cancer vaccine approach and relevant in-vivo efficacy study. These translational researches are supporting a clinical study of AST-301 combining with HER2-ADCs.

REFERENCES