Background IGFBP2, known to enhance the invasion capacity of ovarian cancer cells, has been suggested that its inhibition could be potentially a treatment strategy of ovarian cancer. AST-201 (pUMVC3-hIGFBP2) is a therapeutic cancer vaccine using a plasmid DNA encoding IGFBP2 N-terminus. In a phase 1 study (NCT01322802) completed, 100 µg AST-201 (intradermal immunization, id) showed not only a significant efficacy by inducing the Th1-cell immunity against IGFBP2 but also safety and tolerability profiles in ovarian cancer patients. The primary objective of this study is to evaluate whether the administration of AST-201 alone and the combination with pembrolizumab could show anti-tumor efficacy and/or synergic effect in the ID8-Luc2 ovarian cancer mouse model. Also, immunological responses were observed as explorative endpoint.

Methods AST-201 (100 µg/animal, id, mixed with mGM-CSF as an immune adjuvant) was immunized to mice (C57BL/6) once a week for a total of 3 times on different days, either alongside pembrolizumab (10 mg/kg, intraperitoneal injection) twice a week for a total of 3 times on different days. Also, AST-201 was immunized was a mono treatment. The efficacy was evaluated by a tumor growth inhibition (TGI) rate at the last day, and immune cell profiling via FACS analysis was conducted with splenocytes and tumor tissues collected at 8 weeks after the first injection.

Results As a primary endpoint, a TGI rate at Day 55 of AST-201 mono treatment was 67%, comparing to a control group (p<0.05). The anti-tumor effect of AST-201 combining with pembrolizumab was better than standard dose pembrolizumab, based on a TGI rate at Day 55 (78% vs 66%, not significant). Immune profiling showed that AST-201 and pembrolizumab combination regimen could inhibit a tumor growth by transforming TME into inflamed-type ('hot') form the low immunoactivity, which was supported by increased CD4+TEM and CD8+TEM and T helper cells in splenocyte and TIL analysis.

Conclusions A study demonstrated that AST-201 (IGFBP2 cancer vaccine) showed an anti-tumor effect as mono treatment and would be potentially leading to a synergistic effect with a combination regimen of pembrolizumab. Phase 2 randomized-controlled study of AST-201 in ovarian cancer will be initiated under the MRCT strategy (CornerStone-004 study, NCT05794659).

REFERENCE

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