Abstract

The clinical benefit of monotherapy involving immune checkpoint inhibitors (ICIs) such as anti-programmed death-1 antibody (PD-1 Ab) is limited to small populations. We previously developed a telomerase-specific oncolytic adenovirus, Telomelysin (OBP-301), the safety of which was confirmed in a phase I clinical study. Here, we examined the potential of OBP-502, an OBP-301 variant, as an agent for inducing immunogenic cell death (ICD) and synergistically enhancing the efficacy of OBP-502 with PD-1 Ab using CT26 murine colon cancer and PAN02 murine pancreatic cancer cell lines. OBP-502 induced the release of ICD molecules such as ATP and HMGB1 from CT26 and PAN02 cells, leading to recruitment of CD8-positive lymphocytes and inhibition of Foxp3-positive lymphocyte infiltration into tumors. Combination therapy involving OBP-502 intratumoral administration and PD-1 Ab systemic administration significantly suppressed the growth of not only OBP-502-treated tumors but also tumors not treated with OBP-502 (so-called abscopal effect) in CT26 and PAN02 bilateral subcutaneous tumor models, in which active recruitment of CD8-positve lymphocytes was observed even in tumors not treated with OBP-502. This combined efficacy was similar to that observed in a CT26 rectal orthotopic tumor model involving liver metastases. In conclusion, telomerase-specific oncolytic adenoviruses are promising candidates for combined therapies with ICIs.

Keywords

Immune checkpoint, Programmed death-1, Oncolytic adenovirus, Combined immunotherapy, Immunogenic cell death.