INTRODUCTION

• Published reports have shown that Lm (an intracellular Listeria monocytogenes with LLO fusion peptide) immunotherapies can be combined with different modalities such as radiation, chemotherapy, or immunotherapy for the treatment of cancer.

• ADXS11-001 is a non-viral vector, attenuated, and genetically modified in vitro to secrete an HPV-E7 tumor antigen as tLLO-E7 fusion protein. tLLO refers to the truncated form of non-hemolytic listeriolysin O protein.

• Anti–PD-L1 antibody is a monoclonal antibody that recognizes the PD-L1 protein, which is expressed by tumor cells and acts as a checkpoint inhibitor.

• Due to the unique life-cycle of this bacterium, tLLO-E7 fusion peptide can be used in combination with anti–PD-L1 antibody.

METHODS AND STUDY DESIGN

TUMOR MOUSE MODEL

• TCI cells expressing HPV E7 antigen (1 × 10⁵ cells/mouse) were implanted subcutaneously in the left flank of female (CD-1) nude mice.

TREATMENT AND DOSE

• ADXS11-001 was injected intraperitoneally at a dose of 100 μg/mouse.

• Anti–PD-L1 antibody in a TC1 mouse tumor model.

• Four different treatment groups (1-13) were included in this study:

  - Control group: no treatment
  - ADXS11-001 monotherapy with anti–PD-L1 antibody (total of 3 doses)
  - ADXS11-001 monotherapy with anti–PD-L1 antibody (total of 9 doses)
  - ADXS11-001 + anti–PD-L1 combination therapy (total of 3 doses for ADXS11–001)

RESULTS

ANTI-TUMOR EFFICACY

• The combination of ADXS11-001 (1 × 10⁵ CFU/mouse) and anti–PD-L1 antibody (100 μg) improves the anti-tumor effect compared to the TC1 tumor growth controlled with anti–PD-L1 antibody monotherapy (Figure 3).

IMMUNOLOGIC RESPONSE (CYTOKINES AND CHEMOKINES)

• Several cytokine and chemokine analyses showed that the combination of ADXS11-001 monotherapy or combination therapy (ADXS11-001 + anti–PD-L1) during different days of the study.

• Sharp increases in cytokines (IL-6, IL-10, and IFN-γ) were observed in mice treated with ADXS11-001 monotherapy (Figure 4).

• Macrophage-derived chemokine (MDC) and monocyte inflammatory protein-1 beta (MIP-1β) were observed in mice treated with ADXS11-001 monotherapy (Figure 5).

HYPOThESIS AND STUDY DESIGN

HYPOTHESIS

• Combination of Lm-based immunotherapy with anti-PD-L1 antibody is synergistic, with improved therapeutic responses and prolonged survival without exacerbating potential side effects.

• The combination of Lm-based immunotherapy and anti-PD-L1 blocking antibodies is translatable to the clinical setting for the treatment of malignancies.

METHODS AND STUDY DESIGN

TUMOR MOUSE MODEL

• TCI cells expressing HPV E7 antigen (1 × 10⁵ cells/mouse) were implanted subcutaneously in the left flank of female (CD-1) nude mice.

TREATMENT AND DOSE

• ADXS11-001 was injected intraperitoneally at a dose of 100 μg/mouse.

• Anti–PD-L1 antibody in a TC1 mouse tumor model.

• Four different treatment groups (1-13) were included in this study:

  - Control group: no treatment
  - ADXS11-001 monotherapy with anti–PD-L1 antibody (total of 3 doses)
  - ADXS11-001 monotherapy with anti–PD-L1 antibody (total of 9 doses)
  - ADXS11-001 + anti–PD-L1 combination therapy (total of 3 doses for ADXS11–001)

RESULTS

ANTI-TUMOR EFFICACY

• The combination of ADXS11-001 (1 × 10⁵ CFU/mouse) and anti–PD-L1 antibody (100 μg) improves the anti-tumor effect compared to the TC1 tumor growth controlled with anti–PD-L1 antibody monotherapy (Figure 3).

IMMUNOLOGIC RESPONSE (CYTOKINES AND CHEMOKINES)

• Several cytokine and chemokine analyses showed that the combination of ADXS11-001 monotherapy or combination therapy (ADXS11-001 + anti–PD-L1) during different days of the study.

• Sharp increases in cytokines (IL-6, IL-10, and IFN-γ) were observed in mice treated with ADXS11-001 monotherapy (Figure 4).

• Macrophage-derived chemokine (MDC) and monocyte inflammatory protein-1 beta (MIP-1β) were observed in mice treated with ADXS11-001 monotherapy (Figure 5).

HYPOTHESIS AND STUDY DESIGN

HYPOTHESIS

• Combination of Lm-based immunotherapy with anti-PD-L1 antibody is synergistic, with improved therapeutic responses and prolonged survival without exacerbating potential side effects.

• The combination of Lm-based immunotherapy and anti-PD-L1 blocking antibodies is translatable to the clinical setting for the treatment of malignancies.