Abstract 1218P: Antitumor activity and safety of a novel PD-1 vaccine (PD1-Vaxx) alone and in combination with two chimeric HER-2 peptide vaccine (B-Vaxx) in syngeneic Balb/c mice and canines

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Background
Monoclonal antibodies (mAbs) targeting PD-1 such as Nivolumab or Pembrolizumab have shown activity across a variety of cancers. mAbs such as Herceptin and Perjeta are approved in selected cancers overexpressing HER2. The use of these mAbs is limited by high costs, side effects and development of resistance. In contrast, chimeric B-cell cancer vaccines incorporating a ‘promiscuous’ T-cell epitope could present safer and cheaper alternatives. They elicit a specific immune response that induces memory B & T cell responses, while reducing immune evasion and resistance. We have translated two HER2 combination peptide vaccines (B-Vaxx) to the clinic in a phase 1/2b trial to safely deliver cancer immunotherapies to advanced cancer patients. We have created and established the development of a novel B-cell peptide vaccine (PD1-Vaxx) with high immunogenicity that binds to human PD-1 and produces tumor inhibition in vivo in two animal models of colon cancer. We describe the CT-26 & CT-26/HER-2 tumor models in Balb/c mice used to test for anti-tumor effects of anti-PD-1 immunization therapy alone and in combination with anti-HER2 immunization therapy. The antigenic activity and toxicity profile was investigated in mice and beagle dogs.

Vaccination and Challenge Scheme

Vaccination and Challenge Scheme. Balb/c mice and beagle dogs were immunized with MVF-PD-1 (92-110) peptide vaccine constructs emulsified with ISA 720. Animals were boosted twice at 3 weeks interval. Antibody titers were determined by ELISA. 2 weeks after the final boost 1x10^6 tumor cells from CT26 or CT26/HER-2 tumor lines were transplanted s.c. Control mice either were challenged with 1x10^6 tumor cells and treated with anti-PD-1 antibody (29F.1A12) twice a week for the duration of the experiment.

Antitumor activity of PD-1 and HER-2 combo in CT26 and CT26-HER-2 syngeneic tumor models

CT-26 & CT-26/HER-2 Tumor Challenge in Balb/c mice. Mice were immunized with PD-1 Peptide, 2XHER2 Peptides, triple (2XHER2+PD-1 Peptides) at 3 week’s interval and challenged 10 days after third vaccination. PBS served as negative control and mice treated with anti-mouse PD-1 monoclonal antibody (Mab, 29F.1A12) twice weekly. Tumor volume mm³ (LWH) was measured over the course of 24 days post challenge. One way analysis of variance (one-way ANOVA) and followed by the Tukey’s multiple comparisons test were used to compare data in multiple groups or data between groups in multiple groups by GraphPad (Prism 8.1.2.), n=5-10.

Isotypes of PD-1 vaccination in Balb/c

Immunogenicity of Combination Peptide Vaccines

Results and Conclusions

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- We show robust HER-2 and PD-1 antibody responses in mice and beagle dogs.
- Treatment with PD1-Vaxx and mAb (29F.1A12) had significant reduction in tumor growth in the CT-26 Balb/c model as compared to PBS treated negative controls.
- Combined triple vaccination (PD1-Vaxx and B-Vaxx) was more effective in the CT-26/HER-2 carcinoma cell line in syngeneic Balb/c mice which exhibited superior activity compared to the positive control anti-mouse PD-1 (CD279) mAb.
- The PD-1 vaccine demonstrated antitumor effect in mouse colon cancer showing no evidence of toxicity or autoimmunity in mice, rabbits and canines.
- Combination immunotherapy of HER2 with PD-1 vaccine may offer a promising new approach to control cancer development/progression and could provide improved outcomes while sparing patients the toxicity of chemotherapy.
- A phase 1 clinical trial with the PD-1 vaccine is under planning.

References


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