



A ROLE FOR DOGS IN ADVANCING CANCER IMMUNOTHERAPY RESEARCH

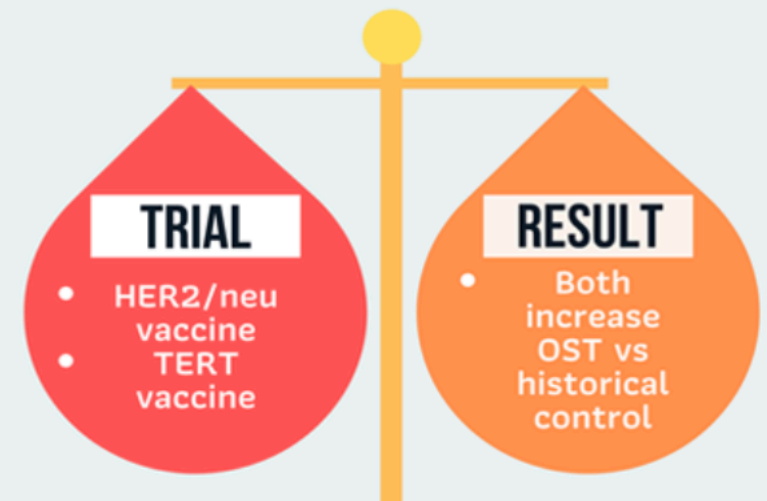
THE CANINE CANCER MODEL AND RELEVANCE TO IMMUNOLOGICAL STUDIES

Dog's immune system in cancer immunotherapy studies already very immunological experienced. They are more broadly 'educated' which will shape the development of antitumor immunity.

COMPARISONS BETWEEN DOGS AND HUMANS IMMUNE CELLS AND IMMUNE RESPONSES

| |  |  |
|--|---|---|
| T cells | CD28, PD-1, OX40, TIGIT, TIM3, Lag3 | CD28, PD-1, OX40, TIGIT, TIM3, Lag3 |
| Ratio of CD4 & CD8T cells in blood and lymph nodes | 2:1 ratio | 2:1 ratio |
| IgG molecules | Four [4] A, B, C, D | Four [4] 2 finding Fc receptors 2 functionally negative |
| Antigen presenting cells | B cells, DC, monocyte, macrophages | MHCII, CD40, CD80, CD86, PD-L1 |

SELECTED CANINE CANCER IMMUNOTHERAPY STUDIES WITH HIGH RELEVANCE TO HUMAN IMMUNO-ONCOLOGY



- Canine osteosarcoma Listeria-vectored vaccine targeting HER2/neu
- Plasmid DNA based tumor vaccine targeting TERT antigen

CANCER VACCINES

ADOPTIVE CELLULAR THERAPY

- ACT with CAR T cells
- ACT with CAR T or CAR NK cells

TUMOR MICROENVIRONMENT MODIFICATION

- Bacterial Super antigen as T cell activator
- Prevent recruitment to tumor issues
- Treatment with an anti-CCR4 antibody
- Administering agents that increase tumor oxygenation

CHECKPOINT MOLECULE TARGETED IMMUNOTHERAPIES

- PD-1
- PD-L1
- OX40

- Viral vectored cytokine delivery approaches
- Systematic administration of IL-12 nanoparticles
- Bacterial delivered therapeutics

OTHER IMMUNOTHERAPY APPROACHES

- Adoptive transfer of non-specifically activated T cells and IL-15 activated NK cells
- Regulatory T cell depletion

THE CHALLENGE FOR IMMUNOTHERAPY

- Lack of necessary immunological reagents
- Large variety of cytokine for dog studies