**GM-CSF**

- **MacEwen et al.** administered to dogs with oral malignant melanoma M-TPP-E alone or in combination with recombinant canine interferon-β. In GM-CSF. Early studies showed a prolonged survival of the dogs. However, there was not an significant antigen activity in advanced stages of canine oral melanoma.

**Fas ligand (FasL)**

- **Dove et al.** treated locally dogs with spontaneous melanoma with platelet-DNA encoding staphylococcal enterotoxin B and other GM-CSF or IL-2. 46% of dogs had complete or partial response. Tumor tumor was infiltrated with macrophages and T lymphocytes. These were increased levels of cytotoxic CD8+ lymphocytes in the bloodstream. Increased survival time was observed and treatment was safe.

**AdCD40L**

- Bianco et al. examined apoptosis of canine melanoma melanoma cells lines in vitro by overexpression of FasL DNA. Overexpression of FasL induced apoptosis in melanoma melanoma cells. Five Fas+ canine melanoma cell lines whereas Fas cell line was resistant. Direct intratumoral administration of FasL DNA to dogs with melanoma was safe and a tumor regression was seen in three out of five dogs.

**HSYk/GCV + IL-2 + GMI-CSFCF**

- **Helfand, Soergel, Donner et al.** assessed the ability of monoclonal antibodies (Mab) targeting CD2 to mediate antigen-dependent cellular toxicity in vitro against a canine melanoma cell line (CM-L10). Monoclonal antibodies potentiating lysis of the canine melanoma cell line by canine peripheral blood lymphocytes (PBL) was stimulated by IL-2.

**IL-2**

- **Helfand et al.** examined the ability of a low dose of human recombinant IL-2 to enhance tumoral properties of canine allogeneic peripheral blood lymphocytes (PBL) in vitro. Human recombinant IL-2 could significantly increase tumor cytotoxicity mediated by canine PBL in vitro, even when used at a concentration unlikely to induce in vivo toxicity in dogs.

**Oncoytic virus**

- **Laborda et al.** treated canine neoplasia using canine melanoma xenograft with a conditionally replicative adenovirus (a canine adenovirus type 2-based oncoytic virus). Treatment resulted in inhibition of tumor growth and prolonged survival of mice. Local administration of the same adenovirus in six tumor-bearing dogs led to two partial responses. There was no direct virus associated adverse effects.

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**CONCLUSION**

The field of tumor immunotherapy is growing rapidly. Melanoma vaccination is having an impressive progress, with new approaches incorporating new antigen targeting and delivery technologies. Recent immunotherapeutic advances against melanoma have been made in human medicine, including anti-CTLA-4 and anti-PD-1 antibodies and adoptive T-cell transfer. Hopefully, in a future, veterinary oncologists will have access to these innovative and effective immunotherapies.

Further research is needed to:

- Understand why some immunotherapies are only effective in some patients
- Improve the immunotherapeutic modalities (maximize efficacy, minimize toxicity and avoid resistance mechanisms)
- Detect reliable biomarkers (e.g. PD-L1) to increase the proportion of patients responding to immunotherapy
- Determine the most effective immunotherapeutic combinations (potential synergistic activity).

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**REFERENCES**