Autologous Activated T cell Therapy for Canine Osteosarcoma

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Canine osteosarcoma (OSA) is an aggressively metastatic primary bone malignancy with frequent chemotherapy failure. We hypothesized that dogs with OSA would be safely treated with autologous vaccination, adoptive cell transfer (ACT) of ex vivo-activated T cells and low dose human interleukin-2 (IL-2) resulting in improved survival compared to current therapeutic options.

Methods

15 tumor bearing dogs were enrolled in a single-arm prospective trial. Dogs were staged with bloodwork, limb and thoracic radiographs, tumor cytology, and bone scans prior to amputation. Autologous vaccinations were administered intradermally at weekly intervals for three weeks and then dogs underwent leukapheresis; mononuclear cell products were stimulated ex vivo. Dogs received ACT followed by five, every other day IL-2 injections subcutaneously. Dogs were monitored for metastasis via thoracic radiographs every three months.

Results

All 15 patients received autologous vaccinations. Eleven dogs received ACT. Dogs developing metastatic disease prior to treatment were dropped from study. One dog did not receive IL-2; ten dogs completed the entirety of the protocol. Most adverse events reported were low grade in nature (Veterinary Cooperative Oncology Group (VCOG) Grade I/II). The most common adverse events after autologous vaccines were transient local reactions and vomiting. The most common adverse events after T cell infusion were transient mild to moderate fever, lethargy, and anorexia. Median disease-free interval for all dogs was 213 days. Median survival time (MST) for all dogs was 339 days. For dogs completing entire protocol, MST = 415 days.

Conclusion

This immunotherapy protocol is safe and tolerable. Compared to historical amputation alone with or without adjuvant chemotherapy, a survival benefit is noted in this group of patients. Further prospective studies are warranted to gain immunologic insight to the protocol and further improve disease response and survival.

ECI®— the only combination adoptive cell therapy available in veterinary oncology

Data presented at Veterinary Cancer Society Annual Conference, October 2018.

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Safety

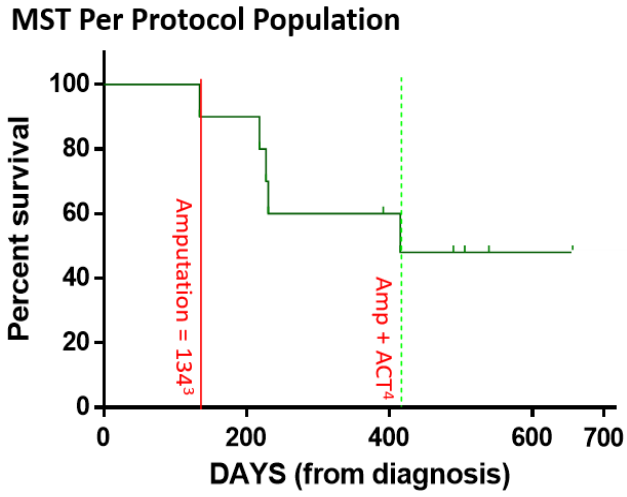
- Except for a single instance of Grade III fever, all reported adverse events were of a low-grade nature (VCOG Grade I/II)
- 15 patients with canine osteosarcoma received autologous vaccinations
- 11 dogs progressed to receive their ex vivo activated T cells
- Ten dogs completed the entirety of the protocol; one dog did not receive adjuvant IL-2
- The most common adverse events after autologous vaccines were transient local reactions and vomiting
- The most common adverse events after ACT infusion were mild to moderate fever, lethargy, and anorexia of a transient nature
- No chemotherapy was administered

Efficacy

- Median disease-free interval for all dogs was 213 days
- Median survival time (MST) for all dogs was 339 days
- Median Survival Time for dogs completing protocol was **415 days**

Kaplan-Meier graph, at right

Includes 5 of 10 dogs which remain disease free and alive as indicated by hashmarks, having survived 390 days or greater post-diagnosis as of October 5, 2018



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[3] Spodnick, et al, 1992.

[4] Flesner, et al, October 2018.

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