

Osteosarcoma Immunotherapy for More Days at Home



Osteosarcoma accounts for $\leq 85\%$ of all primary bone tumors in dogs.¹⁻⁴ Unfortunately, there have been relatively few advancements to create better outcomes for patients suffering from this cancer. In addition, once the current standard of care (ie, amputation plus chemotherapy for patients with limb tumors) fails, there is little hope of survival. That's why studying ELIAS Cancer Immunotherapy (ECI) has been exciting for Jeffrey N. Bryan, DVM, MS, PhD, DACVIM (Oncology), professor of oncology at University of Missouri, and member of the ELIAS Animal Health Scientific Advisory Board.⁵

ECI is the only 2-step immunotherapy in veterinary medicine and has the potential to match or exceed the current standard of care while reducing or eliminating the need for chemotherapy. A form of precision medicine, ECI incorporates both a vaccine pre-treatment made from the patient's cancer cells and an activated "killer" T-cell immunotherapy. The vaccine introduces mutated proteins to the immune system that serve as markers for which cells to eliminate. This generates anticancer lymphocytes that circulate in the blood. After the 3-vaccine pre-treatment, the anticancer lymphocytes are harvested from the patient's blood. ELIAS activates and expands them before they are transfused back into the patient (see **ECI Treatment Protocol**).

Results Backed by Data

Safety and efficacy results support the value of ECI.⁶ Dr. Bryan and his team completed a single-arm, 14-dog pilot study examining ECI osteosarcoma treatment in dogs with no concurrent use of chemotherapy.⁶ ECI showed better survival outcomes than did other treatment options in previous studies.⁶⁻⁸ Dogs receiving ECI survived an average of 415 days, with 5 surviving past 730 days, which exceeds most median survival times historically reported for patients receiving amputation plus chemotherapy.⁶ Few other trials show this proportion of osteosarcoma

patients living this length of time (**Table**, next page).^{5,6,8} Dr. Bryan noted it was rewarding to give patients a better-than-average survival rate and create a greater proportion of long-term survivors.⁵⁻⁸

ECI Hits the Treatment Target

Using the patient's cancer cells to introduce the patient's particular mutations to the immune system is a well-developed anticancer

therapy but, by itself, is rarely successful.⁵ Coupling autologous cancer vaccination with activated T-cell therapy is unique to ECI. As a result, ECI provides the following potential benefits over chemotherapy and standalone autologous cancer vaccination⁵:

- **Eliminates both dividing and dormant cells.** Chemotherapy targets rapidly dividing cells to prevent metastatic disease. Osteosarcoma likely includes a

ECI TREATMENT PROTOCOL

ECI requires fewer appointments as compared with chemotherapy; this and a close partnership between the primary care veterinarian and specialist make the ECI treatment process easier on the client—and the patient.

BEFORE ECI: The primary care veterinarian refers the patient to a veterinary oncologist for aseptic tissue harvesting before amputation. Leaving the limb intact for the oncologist is critical to ensure the collection of viable, plentiful cancer cells. The oncologist performs therapeutic amputation and cell collection before sending tissue to ELIAS for vaccine preparation. ELIAS ships the vaccines back to the oncologist.

WEEKS 1-3: The oncologist administers 3 intradermal injections a week apart with the autologous vaccinations prepared from the collected tissue to generate the appropriate immune response. The injection must be intradermal rather than SC to ensure proper presentation to the immune system.

WEEK 5: The patient visits a specialty apheresis center for leukapheresis, a procedure in which the immune-stimulated T cells are collected from the patient's blood. The oncologist sends these T cells to ELIAS, where technicians prepare the T-cell product, then ship it back to the oncologist.

WEEK 6: The oncologist performs activated T-cell infusion.

WEEKS 7-8: The primary care veterinarian or oncologist performs follow-up interleukin-2 injections. These SC injections are well tolerated and require no specialty training to administer.

large population of metastatic cells not rapidly dividing at the time of treatment. With ECI, cells do not have to be dividing to be eliminated. Instead, they need only to express the mutated abnormal proteins typical of osteosarcoma.

- **Produces durable protection.** Although the underlying immunologic mechanisms involved in ECI are still being investigated, it is possible that the process initiates a population of memory cells that remain in the system.⁶ If cancer cells express the same proteins again, which they tend to do, the immune system can continue to suppress the cancer over time.
- **Powerfully activates cell-killing T cells.** When cancers reach a measurable size, they tend to contain a potentially immunosuppressive microenvironment that protects them from immune attack. Autologous vaccination educates the immune system that cancer cells are abnormal; however, that re-education alone is not enough to overcome the immunosuppressive environment. Literature has shown that most autologous cancer vaccines have failed to induce strong and durable antitumor immunity.⁹ The combination of autologous vaccination and T-cell therapy is critical and associated with the clinical success observed with ECI.
- **Provides more days at home.** The benefits of ECI extend beyond potential treatment success. Chemotherapy often causes severe adverse effects, whereas those associated with ECI are low-grade and transient.⁵ In addition, chemotherapy tends to require longer duration of

therapy as compared with ECI; therefore, ECI requires fewer trips to the veterinarian and allows for more time in the comfort of home.

Referring Veterinarians Play an Active Role

When a primary care veterinarian diagnoses cancer, the next step is to identify the specific cancer type. Aspiration cytology with ALP staining supports the likelihood of bone for tumor origin; this can be performed through radiography to determine tumor location, then through removal of cells with a 22-gauge needle for cytology.

Many veterinarians follow an osteosarcoma diagnosis with immediate leg amputation; ELIAS recommends changing this approach. Immediate amputation eliminates the opportunity to treat with immunotherapy, including ECI. Instead of making amputation the first response, clinicians should consider taking some time to speak with owners about their long-term goals. ECI can provide an alternative to chemotherapy. If owners are interested in ECI, preserving the limb and tumor on the body is vital for ample collection of live cancer cells. With ECI, the specialist performs the amputation, immediately harvesting the tumor and sending the cancer cells to ELIAS for autologous vaccine generation.

Once ECI has been initiated, the general practitioner plays a critical role as the patient's advocate and care team leader. ECI creates a treatment and communication loop among the primary care veterinarian,

oncology specialist, and pet owner and also allows the primary care veterinarian to be highly involved in the treatment process (**Table**). The specialist completes the more intricate aspects of the procedure while the primary care veterinarian manages most of the patient monitoring without the complexities and risks of handling cytotoxic drugs.

Because the primary care veterinarian can be highly involved in supporting the patient through the immunotherapy process, they remain integral to communicating with the pet owner; thus, clients are more likely to contact the primary care veterinarian with questions. They are also likely to return to the primary care veterinarian for vital follow-up visits and any monitoring required (eg, blood tests, radiography). ELIAS Animal Health has resources to guide primary care veterinarians before, during, and after ECI treatment, and practitioners are always welcome to contact ELIAS directly for support.

Hope for Dogs & Their Owners

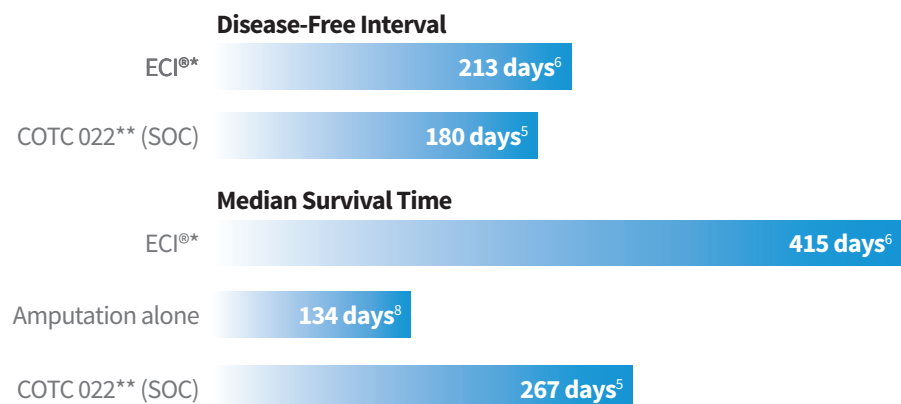
Hearing their dog has cancer of any kind is scary for pet owners. ECI allows veterinarians to help owners of dogs with osteosarcoma decide which options will give their dog the best chance at long-term survival. Although no veterinarian can definitively predict a treatment outcome, data show that immunotherapy tends to result in the highest chance of long-term remission and lowest rate of recurrence across all cancer types.⁹ The ECI trial produced 5 long-term survivors (ie, ≥415 days).⁵⁻⁸

Conclusion

The potential benefits of ECI are significant. Patients bounce back from treatments quickly, and after treatment completion, the only follow-ups required are periodic rechecks. In addition, patients can potentially experience longer survival times, as well as fewer appointments and more days at home when receiving ECI as compared with other treatments,⁵ which can be a major benefit to pet and owner quality of life.

TABLE

ECI TRIAL RESULTS: POWERFUL POTENTIAL



*ELIAS Cancer Immunotherapy

**Comparative Oncology Trials Consortium 022

- ▲ Although the ECI trial was not randomized, it is unusual that, out of 14 dogs selected without particularly restrictive entrance requirements, 5 survived beyond 2 years. This points to the potential power of ECI for treating canine osteosarcoma.

For references, please visit
brief.vet/osteosarcoma

This article was created with the help and expertise of Jeffrey N. Bryan, DVM, MS, PhD, DACVIM (Oncology), professor of oncology at University of Missouri, and member of the ELIAS Animal Health Scientific Advisory Board.⁵ Dr. Bryan's research interests include targeted imaging and therapy and cancer epigenetics and epidemiology. His clinical interests include novel therapy for lymphoma, targeted radiopharmaceutical imaging and therapy, and cancer immunotherapy.



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