ELIAS CANCER IMMUNOTHERAPY (ECI®) TECHNICAL SUMMARY - July 2022

The ELIAS Cancer Immunotherapy (ECI®) is built upon 50+ years of intensive scientific and medical research in rodents, canines and humans. ECI is a type of adoptive cell therapy (ACT) that is designed to stimulate the patient's immune system to recognize cancer cells as "foreign" and then mount an immune response to eliminate them. Unlike other adoptive T cell therapies (e.g., CAR-T, TIL), ECI uses attenuated autologous cancer cell vaccines to "prime" the immune cells to the cancer specific antigens. This approach allows for the harvesting of large numbers of cancer neoantigen specific immune cells. Vaccines manufactured from cancer tissue surgically collected from the patient can prime immune cells to recognize the neoantigens present on the cancer cells. Two weeks after vaccination, primed immune cells are collected from the patient via apheresis for *ex vivo* expansion. The activated T cells are reinfused into the patient and followed by a short series of low dose interleukin-2 injections to further stimulate the immune cells administered.

Efficacy demonstrated in multiple species and cancer types. In pre-clinical rodent models, the ECI approach demonstrated efficacy against a broad range of cancer types including lymphoma, melanoma, prostate, glioma, and others.[1-7] In these preclinical studies, cancers were rejected and in some cases cancer-bearing animals were permanently cured when the activated effector T cells were used to treat minimal disease.[7]

In Phase I/II human clinical trials, the ECI approach has shown efficacy in malignant glioma and renal cell carcinoma patients, with responders having their cancers put into long term remission.[8,9] In humans, this approach being developed by TVAX Biomedical is currently between Phase II/III evaluation for the treatment of glioblastoma multiforme. In 2020, TVAX Biomedical received FDA Fast Track designation for its immunotherapy based in part on key data provided from ELIAS' pilot canine study in osteosarcoma.[10,11] The positive results from ELIAS' study further supported this therapeutic approach as potentially effective in treating multiple cancer types.

Mechanism of action (MOA) has been demonstrated in an *in vitro* study using cancer cells and T cells collected from dogs being treated with ECI for osteosarcoma.[13] In the presence of their respective host cancer cells, activated T cells from vaccinated canines demonstrated cytotoxic activity and generated large levels of proinflammatory cytokines (e.g., IFN-g, TNF-a), important in stimulating an immune response against cancer. Live cell imaging (Figure 1) shows migration and clustering of activated T cells around host cancer cells.

Efficacy and safety treating canine osteosarcoma. Clinical results of a pilot study evaluating ECI in dogs (n=14) with appendicular osteosarcoma were impressive. The median survival times in this single-arm trial was 415 days, with several long-term survivors (Figure 2). These results improved upon previously reported survival results of 134 days for those treated with amputation alone and 308 days for amputation plus chemotherapy[12]. Four out of five long-term surviving dogs lived at least 2 years cancer-free, with the longest living to 5 years post-diagnosis. Another long-term survivor had a distant, cytologically confirmed osteosarcoma metastases for which no further treatment was elected. On recheck two months later, the dog was confirmed to be free of metastasis using a highly sensitive CT/PET scan.[10] This dog survived to 3 years post diagnosis and died of non-cancer causes. Further, ECI continues to demonstrate an excellent safety profile as reported in the pilot study and as seen in current patients.

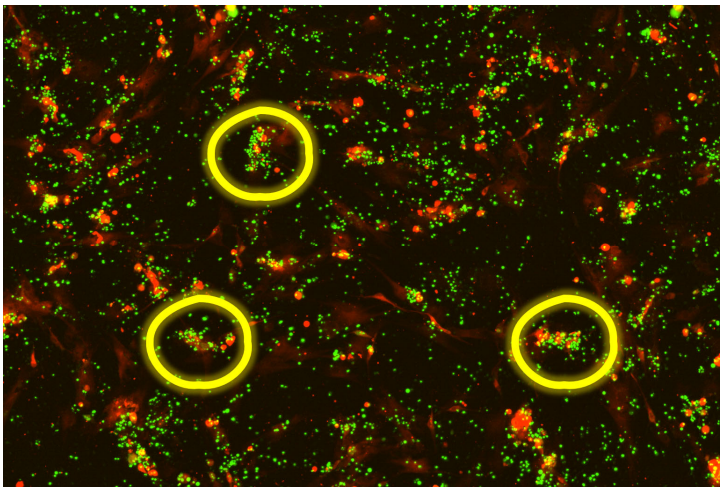

Fig 1. Activated T cells (green) migrating to and clustering around host cancer cells (red). Antigen-specific T cells generate immunostimulatory cytokines and demonstrate cytotoxic activity toward the cancer cells.

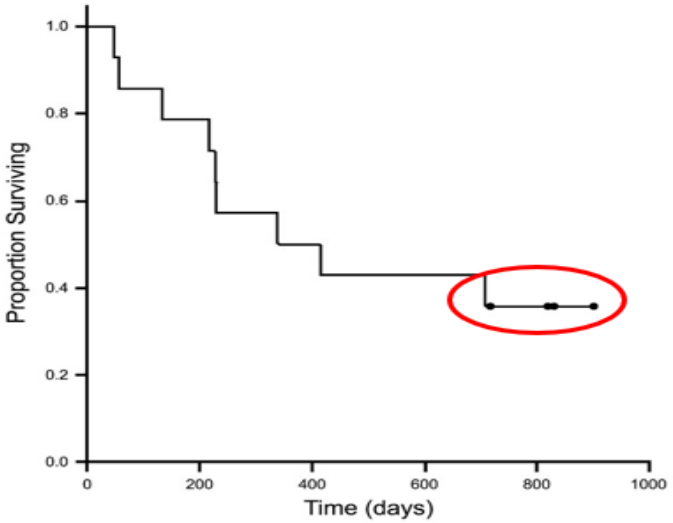

Fig 2. Kaplan Meier curve showing overall survival time for all dogs on an intent-to-treat basis undergoing ECI therapy for osteosarcoma. Overall median survival time (n=14 dogs) was 415 days. Red circle highlights long-term surviving dogs at study conclusion (> 700 days).

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