

Fighting Feline Fibrosarcomas:

An Innovative Therapy



What are fibrosarcomas?

Fibrosarcomas are cutaneous tumors of mesenchymal cell origin that are composed of malignant fibroblasts. They generally originate in the dermal and subcutaneous connective tissue, and are noted to be among the most frequent tumors diagnosed in adult cats.

Fibrosarcoma Characteristics:

- Fibrosarcomas are aggressive tumors, characterized by rapid growth.
- Current standard of care includes early and aggressive surgery; often accompanied by radiotherapy. The efficacy of chemotherapy remains questionable.
- Recurrence is common, even when surgical removal appears complete.

What is Interleukin-2?

- Interleukin-2 (also known as "T cell growth factor") is a glycoprotein secreted by activated T lymphocytes. It stimulates the production of a number of immune cells (including T and B cells), prompts immune cells to be more effective, and causes the cells to increase the production of other cytokines.
- Interleukin-2 has no direct effect on cancer cells, but rather stimulates immune responses involved in the rejection of tumors in cancer patients. When administered in proximity of a tumor, Interleukin-2 has been shown to stimulate an effective tumor-specific immune response.

What is Feline Interleukin-2 Immunomodulator?

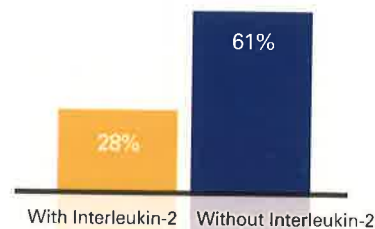
- Feline Interleukin-2 Immunomodulator is conditionally licensed. It is recommended to delay post-surgical recurrence of feline fibrosarcoma in adult cats with stage 1 disease. It utilizes a canarypox vector that has been modified, using recombinant technology, to produce expression of the Feline Interleukin-2 Cytokine that is capable of up-regulating the post-surgical local immune response to feline fibrosarcoma. Safety and reasonable expectation of efficacy of this product have been demonstrated by administration and observation of the time to post-surgical tumor recurrence. Additional efficacy and potency test studies are in progress.

What we know so far

In terms of efficacy, a study by Jourdir et al. (2003) demonstrated the benefits of administration of a canarypox virus vector recombinant expressing feline IL-2 to cats with fibrosarcomas which had been treated with surgery and iridium-based radiotherapy. The treatment led to a decreased likelihood of tumor recurrence (28% of cats in the treatment group, compared with 61% of the cats in the control group). The experimental vaccine used in this study was not a Merial product.

In a European field study, Merial observed a 61.9% recurrence rate within 24 months of surgery and radiotherapy, versus a 29.4% recurrence rate in cats that also received the canarypox-vectored feline IL-2 as an adjunct to surgery and radiotherapy.² There was a trend towards statistical significance ($p=0.052$) for reduction in relapse rate in the IL-2 treated cats. Additional efficacy and potency test studies are in progress.

Recurrence of Fibrosarcoma Post-Surgery and Radiotherapy Using an Experimental Vaccine¹



NOTICE: The USDA has issued a conditional U.S. Veterinary Biological Product License for this therapeutic vaccine. This conditional license is a response to Merial's application supporting safety and purity of the vaccine, in addition to a reasonable expectation of efficacy based on the data described above. During the period of conditional licensure, Merial will pursue further demonstration of efficacy and safety using this vaccine as an adjunct to surgical resection of primary (first occurrence) stage I feline fibrosarcoma. Production under this license is in compliance with all regulations and standards applicable to such products.



¹ Jourdir TM, Moste C, Bonnet MC, et al. Local immunotherapy of spontaneous feline fibrosarcomas using recombinant poxviruses expressing interleukin 2 (IL2). *Gene Therapy*. 2003;10(26):2126-2132.

² Merial. Data on file.

The Newest Way to Fight Feline Fibrosarcomas



Instructions for administration

- Aseptically rehydrate the lyophilized vaccine with 1 mL of the accompanying sterile water diluent, and agitate.
- Cats receive a total of six treatments, with the first administered one week prior to surgical resection of the tumor.
- Administer the second treatment one week post surgery and repeat once a week through the fifth treatment.
- Then wait two weeks and administer the sixth treatment.
- Divide each treatment of a one ml dose into five 0.2 ml injections and administer subcutaneously.
- See below for recommended injection points.
- Use of the recommended mode of administration in five injection points is important for achieving efficacy of the product; injection in one point may lead to reduced efficacy.

Feline Interleukin-2 Immunomodulator Treatment Schedule

WEEKS IN RELATION TO SURGERY	
TREATMENT #1	-1
SURGERY	0
TREATMENT #2	1
TREATMENT #3	2
TREATMENT #4	3
TREATMENT #5	4
TREATMENT #6	6

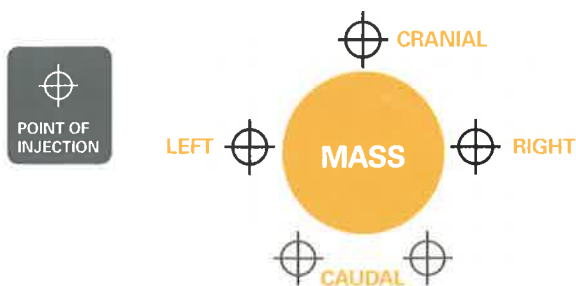
Pre-surgery immunotherapy

The first treatment is given by splitting the 1 ml dose into five separate 0.2 ml injections to be administered subcutaneously at equidistant intervals around the circumference of the tumor. Please see chart below.

Post-surgery immunotherapy

The remaining treatments are given by splitting the 1 ml dose into five separate 0.2 ml injections to be administered subcutaneously, one at each corner of a 5 cm square centered over the surgical scar with the fifth injection near the center of the scar. Please see chart below.

Pre-Surgery Administration Pattern



Post-Surgery Administration Pattern

