

# FidoCure<sup>®</sup>

## Case Study:

### Duchess Thornhill

Left Tonsillar Squamous Cell Carcinoma  
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It is clear that the utilization of targeted therapy has proven beneficial in improving patient quality of life, extending survival time with minimal disease progression, and having an overall positive impact on patient care.



## Introduction

Primary tonsillar cancer is often squamous cell carcinoma, although other cancers such as lymphoma and malignant melanoma can affect the tonsils as well<sup>1</sup>. Cervical lymphadenopathy is a common clinical sign<sup>1</sup>, with regional lymph node metastasis and distant metastasis occurring in up to 75% of cases, while metastasis is observed on thoracic radiographs in about 10–20% of cases at presentation<sup>1</sup>. To confirm diagnosis of tonsillar squamous cell carcinoma, a fine needle aspirate of regional lymph nodes and/or incisional or excisional biopsy of the tonsil is required<sup>1</sup>. Treatment options for tonsillar squamous cell carcinoma include surgical removal of local disease, and radiation therapy in cases where surgery is not possible or if regional lymph node metastasis has occurred and achieving clean margins is not plausible. Due to the high probability of bilateral disease, bilateral tonsillectomy is recommended<sup>1</sup>.

However, it is important to note that both tonsillectomy and cervical lymphadenectomy are almost never curative<sup>1</sup>. Radiation therapy has been shown to control local disease in more than 75% of cases<sup>1</sup>. However, survival rates for tonsillar squamous cell carcinoma are poor, with only about 10% of cases reaching a 1-year survival rate<sup>1</sup>. Surgery or radiation therapy can be followed by intravenous chemotherapy in case of disseminated disease. Currently, there are no known effective chemotherapeutic agents for tonsillar squamous cell carcinoma<sup>1</sup>. One study has shown that radiation therapy combined with chemotherapy was able to improve local tumor control and survival rates in dogs affected with tonsillar squamous cell carcinoma<sup>1</sup>. In another study performed, the combination of surgery, radiation therapy, and/or chemotherapy allowed dogs with tonsillar squamous cell carcinoma to achieve a median survival time of 179 days<sup>1</sup>.

## History, Initial Assessment, and Surgery

Duchess is a 13 year 6 month old female spayed Yorkshire Terrier who was initially diagnosed with left tonsillar squamous cell carcinoma in November of 2019. Duchess has a history of a grade II/VI left apical systolic murmur, pulmonary hypertension, tracheal and mainstem bronchi collapse, keratoconjunctivitis sicca, along with pharyngeal edema and soft palate elongation. Duchess's owner first observed a left-sided cervical mass and lethargy, at which point she presented to VCA ASEC for thoracic radiographs and abdominal ultrasound. A sedated oral exam was performed and biopsy samples were obtained from the mass. Histopathological results from the tonsillar biopsy were consistent with squamous cell carcinoma.

In November 2019, Duchess presented to the VCA West Los Angeles Animal Hospital Surgery service for a second opinion regarding the cervical mass. A CT scan was performed, which revealed left palatine tonsil and left medial retropharyngeal lymphadenopathy/masses. A left-sided tonsillectomy and a left cervical lymphadenectomy were subsequently performed. During the procedure, the lymph node was closely adhered to the carotid artery, which was removed and released via gentle dissection. The left tonsil and cervical mass were submitted for histopathology, which revealed poorly differentiated squamous cell carcinoma with prominent anisocytosis and anisokaryosis and a mitotic index of 19 in the left tonsil and metastatic disease in the left submandibular lymph node.

## Post-Operative Evaluation and Treatment Plan

On December 5th, 2019, Duchess presented for a two-week recheck and suture removal for her left tonsillectomy and left submandibular lymph node removal as well as a consultation with the VCA West Los Angeles Oncology service to discuss available treatment options for tonsillar squamous cell carcinoma. Treatment options such as intravenous chemotherapy, radiation therapy, holistic options including cannabis therapy, Palladia, as well as targeted therapy through FidoCure® were all discussed. FidoCure® utilizes a sample collected from a mass and based on the specific mutations detected in the cancerous tissue, a targeted therapy is recommended. Duchess' owners were not interested in conventional intravenous chemotherapy treatments and elected for treatment with Palladia along with holistic options until the completion of her FidoCure® diagnostic profile. She was started on Palladia and cannabis therapy initially without any adverse effects.

## FidoCure® Analysis

Findings based on RNA expression profile were consistent with overexpression of the CDK4, EGFR, and MYC. CDK4 is the gene encoding cyclin dependent kinase 4. This family of proteins play a critical role in cell cycle regulation, and dysregulation of this pathway can play a role in increased proliferation.

EGFR is the gene encoding epidermal growth factor receptor which is a receptor on the cell surface and is involved with numerous intracellular signaling pathways. Over-expression of this gene may result in tumor cell growth and proliferation through pathways such as MAPK/ERK.

MYC is a gene which codes for intranuclear transcription factors. These proteins are responsible for regulation of various pathways such as cellular growth and proliferation, as well as cellular metabolism.

COX-2 overexpression was also noted on gene analysis which plays a role in the development of prostaglandin E2 (PGE2) which has been shown to promote proliferation, diminish the immune response, and actively reduce signals of apoptosis.

Based on gene expression profile, available targeted therapies, and literature available for using these therapies as treatment options, Lapatinib as an EGFR inhibitor was proposed as a potential targeted therapy. Due to the detection of the overexpression of the COX-2 gene, it was also proposed that utilizing an NSAID in combination with Lapatinib would be beneficial for targeting the cancer from two different aspects.

## FidoCure® Treatment

After receiving gene expression results from the FidoCure® on December 20, 2019, treatment with Lapatinib and meloxicam was initiated, and her progress along with drug tolerance were monitored every two weeks. Upon recheck examination on January 17th, 2020 (approximately two weeks after starting Lapatinib), Duchess did not have any signs of vomiting or diarrhea and was tolerating the medication very well. Her left mandibular lymph node was measured to be 2 X 2 cm and her right mandibular lymph node was slightly enlarged but was presumed to be salivary gland. Lapatinib was subsequently increased from 5 mg/kg/day to its full dose of 10 mg/kg/day and re-staging was performed two weeks later. Curcumin was added one week after increasing the Lapatinib dose. On January 31st, 2020, Duchess presented for a recheck examination and restaging was performed via abdominal ultrasound and thoracic radiographs. Abdominal ultrasound was unremarkable. However, thoracic radiographs revealed ill-defined pulmonary soft tissue nodules in the left caudal lung lobes, which were consistent with possible metastasis to the lungs. Due to the presence of suspect pulmonary nodules, as well as recurrence of the mandibular mass/lymph node, surgery was not recommended and it was advised to pursue consultation for palliative radiation therapy. Owner declined radiation therapy at this time.

On February 28th, 2020, Duchess presented for recheck examination and thoracic radiographs were performed to evaluate progression of previously noted nodules in the lungs. Duchess was reportedly doing well but had occasional coughing at home. At this time, her left mandibular lymph node measured 2.2 X 1.7 cm. Radiographs revealed static disease with subjectively mildly smaller nodules than observed on previously performed radiographs. Due to the static state of her metastatic disease, therapy with Lapatinib and meloxicam was continued. Maitake mushrooms were also added to her therapeutic plan for immune support.

On recheck examination on March 28th, 2020, Duchess was reportedly doing well at home with the exception of a mildly decreased appetite. Her left mandibular lymph node measured 1.8 X 1.7 cm. Recheck thoracic radiographs were obtained and showed static disease in the lungs. Complete blood

work was performed and revealed elevation of ALT at 697 IU/L. It was recommended to discontinue all non-essential medications and administer Zofran once to two times daily until Duchess's appetite improved. If her appetite did not improve, Lapatinib could be discontinued as well.

At her recheck examination in April 2020, Duchess' owners reported that she developed a picky appetite and seemed to have trouble eating on her left side. Attempts at a complete oral examination without sedation were not successful and based on limited visualization of the oral cavity, periodontal disease was diagnosed and Duchess was subsequently prescribed a course of antibiotics for possible oral infection. Recheck echocardiogram was also performed at that time, which revealed worsening of her pulmonary hypertension. Sildenafil was discontinued and it was recommended to administer Tadalafil.

At recheck examination on May 9, 2020, Duchess was doing well, with resolution of her oral issues and weight gain. Her left mandibular lymph node reportedly measured 1.7 X 1.6 cm. Her therapy was continued. Thoracic radiographs performed at her recheck appointment on June 20, 2020 revealed static pulmonary soft tissue nodules. Her left mandibular lymph node was found to be stable if not slightly smaller, measuring 1.7 X 1.5 cm, and it was subsequently recommended to continue her FidoCure® protocol with Lapatinib.

Most recently, Duchess was rechecked on July 31, 2020, at which point her left mandibular lymph node measured 1.6 X 2.2 X 1 cm and palpated more bilobed in nature. Due to the enlargement and bilobed nature of the lymph node, it was recommended to consult with FidoCure® for additional targeted therapy. It was discussed that Lapatinib administration could be continued with the addition of Trametinib at 0.01 mg/kg versus switching to administration of vorinostat. It was elected to move forward with both Lapatinib and Trametinib administration, while administration of the NSAID was discontinued until it could be determined how the new combination of drugs was tolerated. At the time of this report, it is unknown how Duchess has tolerated the new combination of medications. A recheck examination will be performed in two weeks.



## What Duchess' Doctor Says



In my over 10 years of clinical oncology experience, Duchess has significantly surpassed any dog that I have treated with various therapeutic modalities for tonsillar squamous cell carcinoma. I have no doubt that FidoCure®'s precision targeted therapy made all the difference for her."

— Trina Hazzah



## Discussion

Approximately nine months have passed since Duchess' owner first observed her cervical mass. The prognosis for patients with tonsillar squamous cell carcinoma is typically poor, with less than 10% of cases reaching a 1-year survival time. Since surgical excision of the affected tonsil and lymph node as well as administration of targeted therapy with FidoCure®, Duchess has developed pulmonary soft tissue nodules and left mandibular lymph node enlargement. However, her pulmonary disease has remained static and only recently has her left mandibular lymph node become progressively enlarged. Despite the development of pulmonary soft tissue nodules and recurrence of her cervical mass, Duchess has otherwise shown minimal progression of disease for a prolonged period of time, and without the additional use of radiation therapy or typical intravenous chemotherapeutics. The FidoCure® protocol has even been modified to adapt to Duchess's disease progression.

The exact impact FidoCure® has had on patient outcome is currently unknown, as the patient is currently alive and receiving treatment. However, it is clear that the utilization of targeted therapy has proven beneficial in improving patient quality of life, extending survival time with minimal disease progression, and having an overall positive impact on patient care. The role of FidoCure® in the development of individualized therapeutic plans will continue to be an invaluable treatment option in the world of veterinary oncology.

## Literature Cited

1. Withrow, S. J., Vail, D. M., & Page, R. L. (2013). Cancer of the Gastrointestinal Tract. In Withrow & MacEwen's Small Animal Clinical Oncology (5th ed., p. 391). St. Louis, MO: Elsevier.