

# FidoCure<sup>®</sup>

## Case Study:

### Brady Harding

#### Anal Sac Adenocarcinoma

Dr. Dorothy Jackson Girimonte  
VM, DACVIM (Oncology), CVA  
Veterinary Affairs, FidoCure<sup>®</sup>

With the help of FidoCure<sup>®</sup> therapy, Brady lived a great quality of life for 2 years after his initial diagnosis of apocrine gland anal sac adenocarcinoma.



## History and Initial Therapy

Brady Harding, a 8-year-old male neutered Labrador Retriever, was presented to his primary veterinarian in August 2019 for a sedated nail trim. A left-sided anal sac mass was found on physical exam, and cytology was diagnostic for an AGASACA. Thoracic radiographs showed no evidence of metastasis, so the mass was surgically excised. Biopsy confirmed the previous diagnosis of AGASACA. Brady was then referred to MedVet-Norwalk Oncology service. Given the risk of metastasis, Brady's pet parents elected to pursue a course of Carboplatin, along with submitting his biopsy tissue for FidoCure<sup>®</sup> genomic sequencing. He received 4 doses of Carboplatin which were completed in November 2019. Upon completion of injectable chemotherapy, Brady was then routinely monitored every few months for an exam and restaging diagnostics.

## FidoCure<sup>®</sup> Analysis

Tissue from Brady's anal sac tumor was sent for genomic (DNA) and transcriptomic (RNA) sequencing. Genomic analysis revealed alterations of KMT2C and ROS1. KMT2C is a commonly altered gene family in human malignancies. It is a member of the myeloid/lymphoid or mixed-lineage leukemia (MLL) family and encodes a nuclear protein (MLL3). MLL3 is a histone methyltransferase that regulates gene transcription by modifying chromatin structure. KMT2C is also a key regulator of ER $\alpha$  (estrogen receptor) activity whose loss uncouples breast cancer proliferation from hormone abundance (Gala et al., 2018). ROS1 belongs to the sevenless subfamily of tyrosine kinase insulin receptor genes. ROS1 activates several downstream signaling pathways involved in cell differentiation, proliferation, growth and survival, including the PI3 kinase-mTOR signaling pathway.

Findings based on RNA expression profiling were consistent with overexpression of several genes, including CDK4 and ERBB2, and showed potential tumor sensitivity to chemotherapy with platinum-based agents. 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 has been identified as a driver for increased cell proliferation.

ERBB2 (HER2/neu) is a gene that codes for a protein member of the epidermal growth factor (EGF) receptor family of receptor tyrosine kinases. Overexpression of this gene has been implicated in numerous human and canine malignancies. Treatment with an inhibitor of ERBB2 (HER2/neu) may effectively reduce the effects ERBB2 has as potential driver of canine cancer.

## FidoCure® Treatment

When Brady presented for a routine recheck in September 2020, his pet parents reported an episode of flattened stools. Abdominal ultrasound showed sublumbar lymphadenopathy. At that time, he was started on FidoCure® targeted therapy (Lapatinib) based on his initial report. Brady was doing well at his one month recheck in October, and there were no concerns on bloodwork. When he presented in November, he was still doing well, but ultrasound showed progression of his lymphadenopathy. At that time, the decision was made to switch him to Palladia.

Brady did well on targeted therapy for some time. At his recheck in July 2021, radiation therapy was recommended to hopefully obtain better disease control. He started palliative radiation treatment but unfortunately developed severe, left hindlimb lameness half-way through the protocol (November 2021). Bloodwork showed a mild anemia and mild increase in ALP. There was no evidence of metastasis on thoracic radiographs. Radiographs of the hindlimbs showed degenerative changes but no obvious metastasis. MRI showed evidence of bilateral myopathy and neuritis secondary to tumor compression and/or radiation therapy. Brady was hospitalized for supportive care, but he became "down" with difficulty using his hind limbs. Due to a declining quality of life, Brady was ultimately humanely euthanized.

## Conclusion

**On a combined treatment plan, Brady survived 2 years following his initial diagnosis.**

He was still active, even enjoying hiking, just a few weeks before his passing.

## What Brady's Parents Said



...the science gave us time with Brady that we wouldn't have had. We treat our pets as family and therefore take their healthcare seriously. We felt that FidoCure® was human level treatment for Brady.

— Lauren Harding

