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(71) Demandeur/Applicant:
ONEHEALTHCOMPANY, INC., US

(72) Inventeurs/Inventors:
LEWIS, BENJAMIN, US;
LOPES, CHRISTINA KELLY, US;
LAMBERT, LINDSAY, US;
HARVEY, GARRETT, US;
ALLEN, THADDEUS A., US;
MILLER, AUBREY, US;
...

(74) Agent: GOWLING WLG (CANADA) LLP

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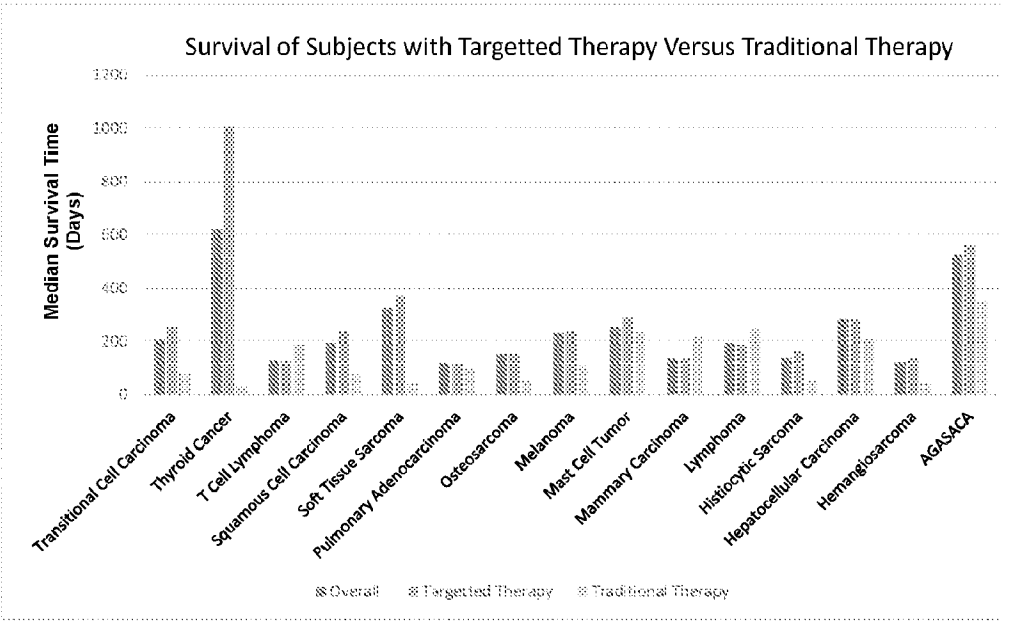


Figure 1

(57) Abrégé/Abstract:
Described herein are methods useful for the treatment of cancers in a canine subject with a pharmaceutical compositions comprising HD AC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof. Also described herein are methods for identification of subjects with cancers that will benefit from administration of the pharmaceutical compositions comprising HD AC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent.

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(72) Inventeurs(suite)/Inventors(continued): RODRIGUES, LUCAS, US; LUKER, MADISON, US; POST, GERALD, US

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(71) Applicant: **ONEHEALTHCOMPANY, INC.** [US/US]; 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US).

(72) Inventors: **LEWIS, Benjamin**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **LOPES, Christina, Kelly**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **LAMBERT, Lindsay**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **HARVEY, Garrett**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **ALLEN, Thaddeus, A.**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **MILLER, Aubrey**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **RODRIGUES, Lucas**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **LUKER, Madison**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US). **POST, Gerald**; C/o Onehealthcompany, Inc., 530 Lytton Ave., Second Floor, Palo Alto, CA 94301 (US).

(74) Agent: **RODRIGUEZ, Elena, M.** et al.; C/o Patent Administrator, Goodwin Procter LLP, 100 Northern Avenue, Boston, MA 02210 (US).

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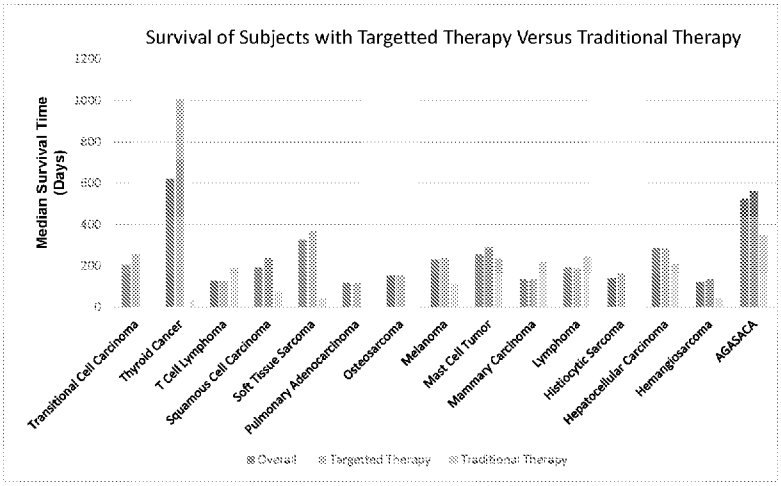


Figure 1

(57) Abstract: Described herein are methods useful for the treatment of cancers in a canine subject with a pharmaceutical compositions comprising HD AC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof. Also described herein are methods for identification of subjects with cancers that will benefit from administration of the pharmaceutical compositions comprising HD AC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent.

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TREATMENT OF CANINE CANCERS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to United States Provisional Application Numbers 62/882,401 filed August 2, 2019; 62/897,872 filed September 9, 2019; 62/898,888 filed September 11, 2019; 62/899,932 filed September 13, 2019; 62/901,185 filed September 16, 2019; 62/902,889 filed September 19, 2019; 62/904,987 filed September 24, 2019; 62/906,924 filed September 27, 2019 and 62/909,098 filed October 1, 2019; which are hereby incorporated by reference in their entirety.

BACKGROUND

[0002] Disclosed herein are methods and compositions useful for the treatment of cancers in a canine subject with various compositions comprising targeted anti-cancer agents, including HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof.

[0003] Rapamycin is an inhibitor of mTOR (mammalian target of Rapamycin), a key protein in the PI3K/Akt pathway that has two different multiprotein complexes: mTORC1 and mTORC2 **(Figure 4).** Increased activation of mTORC1 is observed in numerous cancers due to gain-of-function mutations in oncogenes (e.g., PI3K, AKT, or Ras). mTORC1 serves as a central regulator of cell metabolism, growth, proliferation and survival. Rapamycin has a more complex effect on mTORC2, inhibiting it only in certain cell types under prolonged exposure. Increased activity of PI3K/Akt pathway is often associated with tumor progression and resistance to cancer therapies. Rapamycin binds simultaneously to the FKBP and FRB domains of mTORC1 and acts both upstream and downstream of AKT. S6K1 and 4E-BP1 are two well characterized substrates phosphorylated by mTORC1 implicated in transcription, translation, impacting protein and lipid synthesis and are critical for cell growth and metabolism.

[0004] Dasatinib is an oral synthetic small molecule-inhibitor of SRC-family protein-tyrosine kinases ("SRC family kinases") **(Figure 5**), as well as other tyrosine kinases, including, ABL, BCR-ABL, c-KIT, EPHA2 and PDGFR.. Dasatinib has binding activity to a highly conserved ATP binding site occupancy of which by the drug locks these tyrosine kinases into an inactive state. SRC-family protein-tyrosine kinases and BCR-ABL are non-receptor tyrosine kinases that play important roles in angiogenesis and cellular proliferation of solid and hematological malignancies. SRC family kinases, BCR-ABL and PDGFR play important

roles in regulating mitotic events and activating JAK-STAT, PI3K/AKT and MAPK/ERK signaling pathways that are critical to tumor cells' proliferation and survival. SRC is overexpressed in a variety of solid tumors, while BCR-ABL is the causative agent of canine and human chronic myeloid leukemia (CML).

[0005] Lapatinib is a tyrosine kinase inhibitor that has efficacy in animal models and human clinical trials of cancer where the growth factor receptors ERBB1 (epidermal growth factor receptor, EGFR) and ERBB2 (HER2) contribute to carcinogenesis. The anti-tumor effect of lapatinib is mediated by selective binding to the adenosine triphosphate (ATP) binding pocket of its target receptor tyrosine kinases. This prevents receptor activation through autophosphorylation and prevents further downstream signaling resulting in inhibition of tumor cell proliferation and survival. Lapatinib works high in the EGFR signaling cascade by targeting both the ERBB1 and ERBB2 proteins **(Figure 6).** Lapatinib is able to prevent auto-phosphorylation of these receptor tyrosine kinases, thereby negating downstream signaling cascades. Of particular importance, are the MEK/ ERK and PI3K/AKT pathways that enhance the proliferation and survival of cancer cells.

[0006] Trametinib is a small molecule, non-receptor tyrosine kinase inhibitor. Trametinib is a reversible, selective, allosteric inhibitor of MEK1/MEK2 activation and kinase activity. In vitro studies have demonstrated that trametinib decreases cell proliferation, causes G1 cell cycle arrest, and induces apoptosis. Trametinib inhibits components of one of the MAP kinase cascades that emanate from upstream receptor tyrosine kinases **(Figure 7)**. Depicted here is the epidermal growth factor receptor, but multiple upstream regulators can activate MEK signaling in the same cell. RAS and RAF proto-oncogenes lie proximally in the cascade but even cancers without activated forms of these oncogenes can have constitutive MEK activation.

[0007] Vorinostat is a small molecule, tyrosine kinase inhibitor. Vorinostat is a synthetic hydroxamic acid used orally as a histone deacetylase (HDACs) inhibitor and antineoplasic agent. Vorinostat promotes cell-cycle arrest and apoptosis of cancer cells through regulation of gene expression. Numerous HDACs defects leading to reduced or abnormal acetylation have been identified in leukemia, lymphoma and solid tumor cell lines. These defects include mutation, translocation and overexpression of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1. Vorinostat crosses the blood-brain barrier. Vorinostat inhibits hyperacetylation of histone proteins leading to upregulation of p21 followed by G1 arrest. Hyperacetylation of p53 produces additional anti-proliferative effects. Vorinostat is

recommended in tumors with MYC overexpression due to the regulatory effects on HDACs **(Figure 8).**

[0008] Imatinib is a tyrosine kinase inhibitor used to treat human and animals with cancer. This small molecule works at the ATP binding site of ABL, BCR-ABL, PDGFR, and C-KIT, thereby inhibiting the kinase activity of these proteins. This binding activity blocks downstream signaling that can be important in the maintenance of cell proliferation and survival. Imatinib binds to BCR-ABL, PDGFR and C-KIT, among other targets (**Figure 9**). This can abrogate the ability of these kinases to stimulate mitogen-activated kinases (RAF, MEK and MAPK) and the JAK-STAT and PI3K/AKT pathways. These pathways can be essential in maintaining cell proliferation and survival. Accordingly, this drug can potentially decrease cell proliferation, migration and angiogenesis and enhance apoptosis.

[0009] Crizotinib is a tyrosine kinase inhibitor of ALK, c-MET and ROS1. The formation of ALK-EML4 fusion protein results in the activation of RAS/MAPK, PI3K/AKT, JAK and STAT pathways that play significant roles in cancer development. Crizotinib is able to bind to ALK protein preventing the activation of these downstream pathways. c-MET is a transmembrane tyrosine kinase receptor activated by hepatocyte growth factor (HGF) ligand implicated in the progression of several cancers. The inhibitory effect of crizotinib on c-MET has been shown to inhibit AKT and ERK signaling leading tumor cell to apoptosis. Crizotinib acts on ATP-binding site of ALK-EML4 fusion protein and ROS1. Pathways downstream ALK and ROS1 are PI3K/AKT/ mTOR, JAK/STAT and MAPK/ERK that promote proliferation and cell survival. Crizotinib inhibits c-MET activation avoiding the phosphorylation of adaptor proteins such as GRB2, GAB1, SRC, ShC and c-CBL and subsequente PI3K, AKT, STAT and ERK (**Figure 10**).

[0010] Sorafenib is an oral multikinase inhibitor that targets the 3 RAF serine/threonine kinase isoforms (ARAF, BRAF and CRAF), collectively shown as "Raf" in **Figure 11**, that regulates fundamental cellular processes including growth, differentiation and survival. All RAF proteins are activated by RAS and subsequently activate MEK, initiating the signal transduction cascade of the MAPK pathway. Sorafenib also inhibits the oncogenic BRAF V600E, responsible for abnormal proliferation and differentiation, and tyrosine kinase receptors such as VEGFRs (VEGFR-1, VEGFR-2, VEGFR-3) PDGFR-β,RET and c-KIT (as well as Flt-3, not shown in Figure 11), implicated in tumorigenesis and tumor progression The multisite activity of this small molecule explains its broad preclinical activity across tumor types. Sorafenib blocks receptor tyrosine kinase signaling (VEGFR, PDGFR-β c-KIT

and RET) and inhibits downstream Raf serine/theorine kinase (ARAF, BRAF, mutant BRAF V600E and CRAF) activity to prevent tumor growth by anti-angiogenic, antiproliferative and pro-apoptotic effects. (**Figure 11**).

[0011] Although targeted anti-cancer agents have been effective in the treatment of some human cancers, these agents are generally exhibit unpredictable efficacy, especially. in canines. Therefore, there is a need for improved methods and compositions for predicting efficacy and treating cancers in canine subjects with targeted anti-cancer agents.

SUMMARY

[0012] In certain aspects, described herein is a method of treating a subject with cancer comprising the step of administering a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor to a subject having a cancer harboring at least one mutation in ataxia-telangiectasia mutated (ATM) kinase. In certain embodiments, the method includes the step of identifying the mutation in a sample derived from the subject. In certain embodiments, the HDAC inhibitor is selected from the group consisting of: romidepsin, belinostat, panobinostat, vorinostat, givinostat, entinostat, tacedinaline, and mocetinostat. In certain embodiments, the HDAC inhibitor is vorinostat. In certain embodiments, the method, further comprises administering an effective amount of a DNA damaging chemotherapeutic agent. In certain embodiments, the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain embodiments, the DNA-alkylating agent is selected from the group consisting of: a nitrosourea, a triazene and a platinum agent. In certain embodiments, the DNA-alkylating agent is a nitrosourea. In certain embodiments, the nitrosourea is lomustine. In certain embodiments, the method, further comprises performing surgery on the subject. In certain embodiments, the method further comprises administering an effective amount of at least one additional anti-cancer therapeutic agent. In certain embodiments, the method further comprises administering to the subject ionizing radiation. In certain embodiments, the cancer harbors more than one mutant allele of ATM kinase. In certain embodiments, the biological sample is a nucleic acid sample. In certain embodiments, the biological sample is a purified nucleic acid sample. In certain embodiments, the sample is DNA. In certain embodiments, the sample is RNA. In certain embodiments, the identifying is performed by sequencing a nucleic acid sample. In certain embodiments, the cancer is cancer in a canine subject. In certain embodiments, the cancer is selected from the group consisting of: solid tumor, lymphoma, cutaneous T-cell lymphoma,

peripheral T-cell lymphoma, sarcoma, histiocytic sarcoma, multiple myeloma, hemangiosarcoma, lymphosarcoma, osteosarcoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer and thyroid cancer. In certain embodiments, the cancer is histiocytic sarcoma.

In certain aspects, described herein is a method of treating a subjectwith a cancer harboring at least one mutation in ATM kinase. In certain embodiments, the method further comprises determining or having determined at least one mutation in ATM kinase in a in a sample derived from the cancer. In certain embodiments, the method comprises administering to the subject a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor. In certain embodiments, the HDAC inhibitor is vorinostat. In certain embodiments, the methods further comprise administering a DNA damaging chemotherapeutic agent. In certain embodiments, the DNA damaging chemotherapeutic agent is lomustine. In certain embodiments, at least one mutation in ATM kinase is selected from: a missense mutation, a splice site mutation and a frameshift variant. In certain embodiments, at least one mutation in ATM kinase inhibits ATM kinase activity.

[0013] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Rapamycin. In certain aspects, the Rapamycin is administered at a dose equal to or less than 1 mg/kg. In certain aspects, the Rapamycin is administered at a dose of 0.05-0.1 mg/kg. In certain aspects, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly. In certain aspects, the Rapamycin is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Dasatinib Erlotinib, Gefinitib, Imatinib, Lapatinib, Sorafenib, Trametinib, and Vorinostat. In certain aspects, the targeted anti-cancer agent is Dasatinib. In certain aspects, the methods described herein further comprise performing

surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer. In certain aspects, the cancer is hemangiosarcoma. In certain embodiments, described herein are pharmaceutical compositions formulated for oral administration, comprising Rapamycin, wherein the Rapamycin is present at a concentration of 0.001 mg/mL- 10.0 mg/mL.

[0014] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Dasatinib. In certain aspects, the Dasatinib is administered at a dose equal to or less than 2 mg/kg. In certain aspects, the Dasatinib is administered at a dose of 0.5-0.7 mg/kg. In certain aspects, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5th day, or weekly. In certain aspects, the Dasatinib is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, at least one additional anti-cancer agent is a targeted

anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Lapatinib, Sorafenib, Trametinib, and Vorinostat. In certain aspects, the targeted anti-cancer agent is Rapamycin. In certain aspects, the methods described herein further comprise performing surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer. In certain aspects, the cancer is osteosarcoma. In certain embodiments, described herein are pharmaceutical compositions formulated for oral administration, comprising Dasatinib, wherein the Dasatinib is present at a concentration of 0.001 mg/mL - 10.0 mg/mL.

[0015] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Lapatinib. In certain aspects, the Lapatinib is administered at a dose equal to or less than 50 mg/kg. In certain aspects, the Lapatinib is administered at a dose of 5 mg/kg-10 mg/kg. In certain aspects, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly. In certain aspects, the Lapatinib is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically

effective amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Dasatinib, Sorafenib, Trametinib, and Vorinostat. In certain aspects, the targeted anti-cancer agent is Trametinib. In certain aspects, the methods described herein further comprise performing surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one gene selected from the group consisting of ERBB1 and ERBB2. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ERBB1 and ERBB2. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain aspects, the cancer is transitional cell carcinoma. In certain embodiments, described herein are pharmaceutical compositions formulated for oral administration, comprising Lapatinib, wherein the Lapatinib is present at a concentration of 0.001 mg/mL - 100.0 mg/mL.

[0016] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Trametinib. In certain aspects, the Trametinib is administered at a dose equal to or less than 0.05 mg/kg/day. In certain aspects, the Trametinib is administered at a dose of 0.02 mg/kg/day. In certain aspects, the

pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5th day, or weekly. In certain aspects, the Trametinib is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetbolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Dasatinib, Sorafenib, Lapatinib, and Vorinostat. In certain aspects, the targeted anti-cancer agent is Rapamycin. In certain aspects, the targeted anti-cancer agent is Dasatinib. In certain aspects, the targeted anti-cancer agent is Lapatinib. In certain aspects, the methods described herein further comprise performing surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one gene selected from the group consisting of MEK1 and MEK2. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of MEK1 and MEK2. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma). In certain embodiments, described herein are pharmaceutical compositions formulated for

oral administration, comprising Trametinib, wherein the Trametinib is present at a concentration of 0.001 mg/mL - 100.0 mg/mL.

[0017] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Vorinostat. In certain aspects, the Vorinostat is administered at a dose equal to or less than 100 mg/kg. In certain aspects, the Vorinostat is administered at a dose of 30-60 mg/kg. In certain aspects, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5th day, or weekly. In certain aspects, the Vorinostat is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Dasatinib, Sorafenib, Lapatinib, and Trametinib. In certain aspects, the targeted anti-cancer agent is Rapamycin. In certain aspects, the targeted anti-cancer agent is Trametinib. In certain aspects, the targeted anti-cancer agent is Lapatinib. In certain aspects, the methods described herein further comprise performing surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer overexpresses MYC. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in at least one gene is

performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma). In certain aspects, the cancer is hemangiosarcoma. In certain aspects, the cancer is histiocytic sarcoma. In certain embodiments, described herein are pharmaceutical compositions formulated for oral administration, comprising Vorinostat, wherein the Vorinostat is present at a concentration of 0.01 mg/mL - 500.0 mg/mL.

[0018] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Imatinib. In certain aspects, the Imatinib is administered at a dose equal to or less than 50 mg/kg. In certain aspects, the Imatinib is administered at a dose of 10 mg/kg. In certain aspects, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly. In certain aspects, the Imatinib is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, the at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Sorafenib, Trametinib, and Vorinostat. In certain aspects, the targeted anti-cancer agent is Trametinib. In certain aspects, the targeted anti-cancer agent is Rapamycin. In certain aspects, the methods described herein further comprise performing surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one

gene selected from the group consisting of ABL, BCR-ABL, PDGFR, and C-KIT. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, PDGFR, and C-KIT. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain aspects, the cancer is hemangiosarcoma. In certain aspects, the cancer is mast cell tumors. In certain embodiments, described herein are pharmaceutical compositions formulated for oral administration, comprising Imatinib, wherein the Imatinib is present at a concentration of 0.01 mg/mL - 100.0 mg/mL.

[0019] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Crizotinib. In certain aspects, Crizotinib is administered at a dose equal to or less than 10 mg/kg. In certain aspects, Crizotinib is administered at a dose of 1 mg/kg- 2 mg/kg. In certain aspects, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly. In certain aspects, Crizotinib is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from

the group consisting of: Imatinib, Rapamycin, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Sorafenib, Trametinib, and Vorinostat. In certain aspects, the targeted anti-cancer agent is Trametinib. In certain aspects, the targeted anti-cancer agent is Imatinib. In certain aspects, the methods described herein further comprise performing surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one gene selected from the group consisting of ALK, c-MET and ROS1. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ALK, c-MET and ROS1. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain aspects, the cancer is hemangiosarcoma. In certain aspects, the cancer is osteosarcoma. In certain embodiments, described herein are pharmaceutical compositions formulated for oral administration, comprising Crizotinib, wherein Crizotinib is present at a concentration of 0.01 mg/mL - 100.0 mg/mL.

[0020] In certain embodiments, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Sorafenib. In certain aspects, the Sorafenib is administered at a dose of less than 10 mg/kg. In certain aspects, the Sorafenib is administered at a dose of 1 mg/kg- 3 mg/kg. In certain aspects, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly. In certain aspects, the Sorafenib is administered orally. In certain aspects, the methods described herein further comprise administering a therapeutically effective

amount of at least one additional anti-cancer agent. In certain aspects, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain aspects, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain aspects, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain aspects, the targeted anti-cancer agent is selected from the group consisting of: Imatinib, Rapamycin, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Crizontinib, Trametinib, and Vorinostat. In certain aspects, the targeted anti-cancer agent is Imatinib. In certain aspects, the methods described herein further comprise performing surgery on the subject. In certain aspects, the methods described herein further comprise administering to the subject ionizing radiation. In certain aspects, the cancer harbors at least one mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB. In certain aspects, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB. In certain aspects, the biological sample is a nucleic acid sample. In certain aspects, the biological sample is a purified nucleic acid sample. In certain aspects, the sample is DNA. In certain aspects, the sample is RNA. In certain aspects, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain aspects, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain aspects, the cancer is mast cell tumor. In certain aspects, the cancer is osteosarcoma. In certain embodiments, described herein are pharmaceutical compositions formulated for oral administration, comprising Sorafenib, wherein the Sorafenib is present at a concentration of 0.01 mg/mL - 100.0 mg/mL.

[0021] In certain aspects of the methods described herein, the cancer harbors at least one mutation in at least one gene shown in Tables 1, 2 and 12-26. In certain embodiments, the methods further comprise determining or having determined from a biological sample

derived from the cancer, at least one mutation in at least one gene shown in Tables 1, 2, and 12-26.

[0022] In certain aspects of the methods described herein, the cancer has increased or decreased expression in at least one gene shown in Tables 1, 2 and 12-26 compared to non-cancerous tissue. In certain embodiments, the methods further comprise determining or having determined from a biological sample derived from the cancer, increased or decreased expression in at least one gene shown in Tables 1, 2, and 12-26 compared to non-cancerous tissue.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

[0023] These and other features, aspects, and advantages of the present invention will become better understood with regard to the following description, and accompanying drawings, where:

[0024] Figure 1: is a graph showing the median survival of subjects treated with targeted therapies comprising, HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof according to the present disclosure versus subjects treated with traditional non-targeted therapies.

[0025] Figure 2 is a graph showing Kaplan-Meier survival of canine subjects with splenic hemangiosarcoma that have been either treated with chemotherapy and splenectomy alone ("control") or treated with targeted therapy and chemotherapy and splenectomy ("treated").

[0026] Figure 3 is a graph showing Kaplan-Meier survival of canine subjects with Transitional Cell Carcinoma (TCC) and/or Urinary Cancer (UC) harboring a BRAF mutation. Dogs treated with targeted drugs (Trametinib, Lapatinib or Lapatinib and Trametinib) with or without standard chemotherapy and a COX2 inhibitor exceeded published median survival times (MST) for either Cox inhibitor treatment alone (195 days) or chemotherapy and Cox2 inhibitor treatment (291 days).

[0027] Figure 4 is an illustration of mechanisms of Rapamycin action in cancer cell signaling. Rapamycin binds to mTORC1 and acts both upstream and downstream of AKT. S6K1 and 4E-BP1 are two well characterized substrates phosphorylated by mTORC1 implicated in transcription, translation, protein, lipids synthesis and is found to be critical for cell growth and metabolism.

[0028] Figure 5: is an illustration of mechanisms of Dasatinib action in cancer cell signaling. Dasatinib has binding activity to a highly conserved ATP binding site to lock the tyrosine kinase in an inactive state. Dasatinib inhibits SRC family kinases, BCR-ABL, KIT, and

PDGFR that play important roles in regulating mitotic events and activating JAK-STAT, PI3K/AKT and MEK/ERK signaling pathways that are critical to tumor cells' proliferation and survival.

[0029] Figure 6: is an illustration of mechanisms of Lapatinib action in cancer cell signaling. Lapatinib is able to prevent auto-phosphorylation of these receptor tyrosine kinases (e.g., EGFR and HER2), thereby negating downstream signaling cascades. Of particular importance, are the MEK/ ERK and PI3K/AKT pathways that enhance the proliferation and survival of cancer cells.

[0030] Figure 7: is an illustration of mechanisms of Trametinib action in cancer cell signaling. Trametinib inhibits, MEK, a component of the MAP kinase cascade, that is activated by upstream receptor tyrosine kinases. Depicted here is the epidermal growth factor receptor, but multiple upstream regulators can activate MEK signaling in the same cell. RAS and RAF proto-oncogenes lie proximally in the cascade but even cancers without activated forms of these oncogenes can have constitutive MEK activation.

[0031] Figure 8: is an illustration of mechanisms of Vorinostat action in cancer cell signaling. Vorinostat inhibits hyperacetylation of histone proteins leading to cell cycle arrest of cancer cells with activated MEK/ERK and/or PI3K/AKT pathways.. Vorinostat is recommended in tumors with MYC overexpression due to the regulatory effects on HDACs.

[0032] Figure 9: is an illustration of mechanisms of Imatinib action in cancer cell signaling. Imatinib is able to prevent auto-phosphorylation of KIT, and PDGFR receptor tyrosine kinases, and Bcr-Abl non-receptor tyrosine kinase, thereby negating downstream signaling cascades. Of particular importance, are the MEK/ ERK and PI3K/AKT pathways that enhance the proliferation and survival of cancer cells.

[0033] Figure 10: is an illustration of mechanisms of Crizotinib action in cancer cell signaling. Crizotinib acts on ATP-binding site of ALK-EML4 fusion protein and ROS1. Pathways downstream ALK and ROS1 include: PI3K/AKT/, JAK/STAT and MEK/ERK that promote proliferation and cell survival. Crizotinib inhibits c-MET activation avoiding the phosphorylation of adaptor proteins such as GRB2, GAB1, SRC, ShC and c-CBL and subsequent inhibition of activation of PI3K, AKT, STAT and ERK.

[0034] Figure 11: is an illustration of mechanisms of Sorafenib action in cancer cell signaling. Sorafenib blocks receptor tyrosine kinase signaling (VEGFR, PDGFR-β, c-KIT and RET) and inhibits downstream Raf serine/threonine kinases (ARAF, BRAF, mutant

BRAF V600E and CRAF) activity to prevent tumor growth by anti-angiogenic, antiproliferative and pro-apoptotic effects.

[0035] Figure 12: is an illustration showing the analysis of ATM mutations in The Cancer Genome Atlas (TCGA), Pan Cancer Atlas. **TOP:** Information available through cBioPortal for Cancer Genomics (https://www.cbioportal.org/) was used to examine the spectrum of ATM mutations in human cancer. Mutations appear across the coding sequence with few hotspots. Of 10967 tumor samples from 32 histologies, 554 (5.1%) harbored mutations in ATM. **BOTTOM:** Pattern of mutation observed in canine cancer in the dataset. Mutations appear across histologies and like the human gene, interspersed along the coding sequence. Mutation was observed in 7.65% of tumors. The Ala989Val mutation occurs in Labrador Retrievers and Labrador mixed breed dogs and may therefore be an unconfirmed SNP of unknown functional significance. TAN: Tel1/ATM N-Terminal motif, FAT: FRAP-ATM-TRRAP interaction domain, PIKKc: PI3K-related serine/threonine protein kinase domain.

DETAILED DESCRIPTION

[0036] Briefly, and as described in more detail below, described herein are methods useful for the treatment of cancer in a canine subject with a pharmaceutical compositions comprising HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof. Also described herein are methods for identification or selection of subjects with cancers that are likely to derive significant therapeutic responses to administration of the pharmaceutical compositions comprising HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof. The methods of the present disclosure are useful for treating subjects with cancer with targeted therapies comprising HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof for increasing survival of the subjects compared to traditional therapies (**Figure 1 and Table 1**). In certain aspects, the methods herein cause increased survival of a subject with cancer following treatment with the targeted therapies disclosed herein compared to traditional chemotherapy (**Figures 2 and 3**).

Definitions

[0037] Terms used in the claims and specification are defined as set forth below unless otherwise specified.

[0038] The term "canine cancer" can refer to any cancer, tumor or hyperproliferative disorder that is present in a canine subject. In embodiments, the canine cancer is a specified cancer that is surprisingly responsive to one or more of the treatments described in this disclosure.

[0039] The term "treating" refers to any therapeutically beneficial result in the treatment of a disease state, e.g., a cancer disease state, including lessening in the severity or progression, remission, or cure thereof.

[0040] The term "sufficient amount" means an amount sufficient to produce a desired effect, e.g., an amount sufficient to modulate protein aggregation in a cell.

[0041] The term "therapeutically effective amount" is an amount that is effective to ameliorate a symptom of cancer or hyperproliferative disease.

[0042] The term "anti-cancer agent" refers to, but is not limited to chemotherapeutic agents, targeted therapies, hormones, and immunotherapies. Anti-cancer agents can be, but are not limited to, a small molecule, an antibody or antibody fragment, nucleic acid (e.g., DNA or RNA), carbohydrates, peptides, lipids, exosomes, cells, or combinations thereof.

[0043] The term "targeted anti-cancer agent" refers to, but is not limited to, anti-cancer agents that specifically alter a cancer cell characteristic (e.g., an agent that interacts with a gene product, such as a protein or RNA, that regulates a cancer cell characteristic, such as cell proliferation, cell survival, metastasis, immune evasion, etc.).

[0044] The term "overexpression" when referring to a gene (e.g., an oncogene such as MYC), refers to increased amounts of mRNA or protein with respect to a non-cancer tissue control sample. A gene can be considered overexpressed when the mRNA and/or protein amounts of the gene are greater than 2.0 fold, 5 fold, 10 fold, 20 fold, 30 fold, 40 fold, 50 fold, 60 fold, 70 fold, 80 fold, 90 fold, 100 fold, 150 fold, 200 fold 300 fold, 400 fold 500 fold or 1000 fold the amount of RNA and/or protein of a non-cancer tissue control sample. In certain embodiments, the gene is overexpressed when the mRNA and/or protein amounts of the gene are 2 fold to 10 fold, 5 fold to 10 fold, 10 fold to 100 fold, 10 fold to 50 fold, 50 fold to 100 fold, or 100 fold to 1000 fold greater than the amount of RNA and or protein of a non-cancer tissue control sample. Overexpression can be determined by any appropriate method known in the art, including, but not limited to, RNA SEQ, and quantitative PCR, immunohistochemistry.

[0045] The term "underexpression" when referring to a gene (e.g.,a tumor surpressor gene such as p53), refers to decreased amounts of mRNA or protein with respect to a non-cancer tissue control sample. A gene can be considered underexpressed when the mRNA and/or

protein amounts of the gene are less than 2.0 fold, 5 fold, 10 fold, 20 fold, 30 fold, 40 fold, 50 fold, 60 fold, 70 fold, 80 fold, 90 fold, 100 fold, 150 fold, 200 fold 300 fold, 400 fold 500 fold or 1000 fold the amount of RNA and/or protein of a non-cancer tissue control sample. In certain embodiments, the gene is underexpressed when the mRNA and/or protein amounts of the gene are 2 fold to 10 fold, 5 fold to 10 fold, 10 fold to 100 fold, 10 fold to 50 fold, 50 fold to 100 fold, or 100 fold to 1000 fold less than the amount of RNA and or protein of a non-cancer tissue control sample. Underexpression can be determined by any appropriate method known in the art, including, but not limited to, RNA SEQ, and quantitative PCR, immunohistochemistry.

[0046] Abbreviations used in this application include the following: HDAC (histone deacetylase), ATM, mTOR, PI3K, AKT, Ras, ABL, BCR-ABL, c-KIT, EPHA2, PDGFR, a Src Family Kinase, ERBB1, ERBB2, MEK1, MEK2, p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5, HDAC1, MYC, ALK, c-MET, ROS1, RAF, FLT-3, RET, VEGFRs and PDGFRB.

[0047] ATM is also known as ataxia-telangiectasia mutated (ATM) kinase, Serine-Protein kinase ATM, A-T Mutated, TEL1, and Telomere Maintenance 1 Homolog. Canis lupus familiaris (canine) PDGFRB is encoded by the gene having an Ensembl identification number of: ENSCAFG00000014454.

[0048] mTOR is also known as, Mechanistic Target Of Rapamycin Kinase, Mammalian Target Of Rapamycin, Rapamycin And FKBP12 Target 1, FK506-Binding Protein 12-Rapamycin Complex-Associated Protein 1, Mechanistic Target Of Rapamycin (Serine/Threonine Kinase), FK506 Binding Protein 12-Rapamycin Associated Protein 2, FKBP12-Rapamycin Complex-Associated Protein 1, Serine/Threonine-Protein Kinase MTOR, Rapamycin Associated Protein FRAP2, FKBP-Rapamycin Associated Protein, Mechanistic Target Of Rapamycin, Rapamycin Target Protein 1, FRAP1, RAFT1, FRAP, DJ576K7.1 (FK506 Binding Protein 12-Rapamycin Associated Protein 1), FK506 Binding Protein 12-Rapamycin Associated Protein 1, FKBP12-Rapamycin Complex-Associated Protein, Rapamycin Target Protein, EC 2.7.11.1, MTOR, or SKS. Canis lupus familiaris (canine) mTOR is encoded by the gene having an Ensembl identification number of: ENSCAFG00000016648.

[0049] PI3K refers to the family of kinases also known as Phosphoinositide 3-kinases or phosphatidylinositol 3-kinases.

[0050] AKT refers to AKT Serine/Threonine Kinase 1, V-Akt Murine Thymoma Viral Oncogene Homolog 1, RAC-Alpha Serine/Threonine-Protein Kinase, Protein Kinase B Alpha, Proto-Oncogene C-Akt, Protein Kinase B, RAC-PK-Alpha, EC 2.7.11.1, PKB Alpha, PKB, and RAC. Canis lupus familiaris (canine) AKT1 is encoded by the gene having an Ensembl identification number of: ENSCAFG00000018354.

[0051] ABL is also known as ABL Proto-Oncogene 1, Non-Receptor Tyrosine Kinase, V-Abl Abelson Murine Leukemia Viral Oncogene Homolog 1, C-Abl Oncogene 1, Receptor Tyrosine Kinase, Abelson Tyrosine-Protein Kinase 1, Tyrosine-Protein Kinase ABL1, Proto-Oncogene C-Abl, EC 2.7.10.2, JTK7, and P150. Canis lupus familiaris (canine) ABL is encoded by the gene having an Ensembl identification number of: ENSCAFG00000019938.

[0052] BCR-ABL is also known as BCR-ABL Major-Breakpoint Cluster Region; BCR P210 Philadelphia Chromosome Recombination Region, T(9;22)(Q34;Q11) M-BCR Recombination Region, and BCR P210 Breakpoint Recombination Region.

[0053] c-KIT is also known as KIT Proto-Oncogene, Receptor Tyrosine Kinase, V-Kit Hardy-Zuckerman 4 Feline Sarcoma Viral Oncogene Homolog, Mast/Stem Cell Growth Factor Receptor Kit, Tyrosine-Protein Kinase Kit, Piebald Trait Protein, Proto-Oncogene C-Kit, EC 2.7.10.1, P145 C-Kit, SCFR, PBT, V-Kit Hardy-Zuckerman 4 Feline Sarcoma Viral Oncogene-Like, Proto-Oncogene Tyrosine-Protein Kinase Kit, Soluble KIT Variant 1, C-Kit Protooncogene, CD117 Antigen, Piebald Trait, EC 2.7.10, C-Kit, CD117, and MASTC. Canis lupus familiaris (canine) c-Kit is encoded by the gene having an Ensembl identification number of: ENSCAFG00000002065.

[0054] EPHA2 is also known as EPH Receptor A2, Tyrosine-Protein Kinase Receptor ECK, Ephrin Type-A Receptor 2, EC 2.7.10.1, ECK, Epithelial Cell Receptor Protein Tyrosine Kinase, Soluble EPHA2 Variant 1, Epithelial Cell Kinase, EC 2.7.10, CTRCT6, ARCC2, CTPP1, EphA2, and CTPA. Canis lupus familiaris (canine) EPHA2 is encoded by the gene having an Ensembl identification number of: ENSCAFG00000016011.

[0055] PDGFR includes PDGFRA and PDGFRB. PDGFRA is also known as Platelet Derived Growth Factor Receptor Alpha, Platelet-Derived Growth Factor Receptor, Alpha Polypeptide, Alpha-Type Platelet-Derived Growth Factor Receptor, Platelet-Derived Growth Factor Receptor Alpha, Platelet-Derived Growth Factor Receptor 2, CD140 Antigen-Like Family Member A, CD140a Antigen, PDGF-R-Alpha, and EC 2.7.10.1. Canis lupus familiaris (canine) PDGFRA is encoded by the gene having an Ensembl identification number of: ENSCAFG00000002057. PDGFRB is also known as Platelet Derived Growth

Factor Receptor, Beta Platelet-Derived Growth Factor Receptor, Beta Polypeptide, Beta-Type Platelet-Derived Growth Factor Receptor, Platelet-Derived Growth Factor Receptor Beta, Platelet-Derived Growth Factor Receptor 1, CD140 Antigen-Like Family Member B, PDGF-R-Beta, EC 2.7.10.1, PDGFR-Beta, PDGFR-1, PDGFR1, PDGFR, Beta Platelet-Derived Growth Factor Receptor, Activated Tyrosine Kinase PDGFRB , CD140b Antigen, NDEL1-PDGFRB, EC 2.7.10, CD140B, IBGC4, JTK12, PENTT, IMF1, and KOGS. Canis lupus familiaris (canine) PDGFRB is encoded by the gene having an Ensembl identification number of: ENSCAFG00000018214.

[0056] Src Family Kinase refers to non-receptor tyrosine kinases that includes: Src, Yes, Fyn, and Fgr, forming the SrcA subfamily, Lck, Hck, Blk, and Lyn and Frk.

[0057] ERBB1 is also referred to as Epidermal Growth Factor Receptor, Receptor Tyrosine-Protein Kinase ErbB-1, Erb-B2 Receptor Tyrosine Kinase 1, Proto-Oncogene C-ErbB-1, EC 2.7.10.1, ERBB1, ERBB, HER1, Epidermal Growth Factor Receptor (Avian Erythroblastic Leukemia Viral (V-Erb-B) Oncogene Homolog), Erythroblastic Leukemia Viral (V-Erb-B) Oncogene Homolog (Avian), Avian Erythroblastic Leukemia Viral (V-Erb-B) Oncogene Homolog, Epidermal Growth Factor Receptor Tyrosine Kinase Domain, Cell Proliferation-Inducing Protein 61, Cell Growth Inhibiting Protein 40, EC 2.7.10, NISBD2, PIG61 and MENA. Canis lupus familiaris (canine) ERRB1 is encoded by the gene having an Ensembl identification number of: ENSCAFG00000003465.

[0058] ERBB2 is also known as: Erb-B2 Receptor Tyrosine Kinase 2, V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 2, Tyrosine Kinase-Type Cell Surface Receptor HER2, Neuro/Glioblastoma Derived Oncogene Homolog, Human Epidermal Growth Factor Receptor 2, Receptor Tyrosine-Protein Kinase ErbB-2, Metastatic Lymph Node Gene 19 Protein, Proto-Oncogene C-ErbB-2, Proto-Oncogene Neu, EC 2.7.10.1, P185erbB2, MLN 19, HER2, NGL, NEU, V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 2 (Neuro/Glioblastoma Derived Oncogene Homolog), V-Erb-B2 Erythroblastic Leukemia Viral Oncogene Homolog 2, Neuro/Glioblastoma Derived Oncogene Homolog, V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncoprotein 2, Neuroblastoma/Glioblastoma Derived Oncogene Homolog, C-Erb B2/Neu Protein, CD340 Antigen, HER-2/Neu, Herstatin, EC 2.7.10, CD340, HER-2, MLN19, and TKR1. Canis lupus familiaris (canine) ERRB2 is encoded by the gene having an Ensembl identification number of: ENSCAFG00000016351.

[0059] MEK1 is also referred to as Mitogen-Activated Protein Kinase Kinase 1, MAP2K1, Dual Specificity Mitogen-Activated Protein Kinase Kinase 1, ERK Activator Kinase 1, MAPK/ERK Kinase 1, EC 2.7.12.2, MAPKK 1, MKK1 and PRKMK1. Canis lupus familiaris (canine) MEK1 is encoded by the gene having an Ensembl identification number of: ENSCAFG00000017298.

[0060] MEK2 is also known as: Mitogen-Activated Protein Kinase Kinase 2, MAP2K2, Dual Specificity Mitogen-Activated Protein Kinase Kinase 2, ERK Activator Kinase 2, MAP Kinase Kinase 2, MAPK/ERK Kinase 2, EC 2.7.12.2, PRKMK2, MKK2, Mitogen-Activated Protein Kinase Kinase 2, P45, MAPKK 2, and MAPKK2. Canis lupus familiaris (canine) MEK2 is encoded by the gene having an Ensembl identification number of: ENSCAFG00000019138.

[0061] P300 is also referred to as: E1A Binding Protein P300, Histone Acetyltransferase P300, Protein Propionyltransferase P300, Histone Crotonyltransferase P300, Histone Butyryltransferase P300, E1A-Associated Protein P300, EC 2.3.1.48, P300 HAT, E1A-Binding Protein, 300kD, EC 2.3.1, EC 2.3.1, KAT3B, MKHK2, and RSTS2. Canis lupus familiaris (canine) p300 is encoded by the gene having an Ensembl identification number of ENSCAFG00000001125.5

[0062] CBP is also referred to as: CREBBP, CREB-Binding Protein, KAT3A, MKHK1, RSTS1, and RSTS. Canis lupus familiaris (canine) CBP is encoded by the gene having an Ensembl identification number of ENSCAFG00000019251.

[0063] TIF-2 is also referred to as NCOA2, Nuclear Receptor Coactivator 2; Class E Basic Helix-Loop-Helix Protein 75, Transcriptional Intermediary Factor 2, BHLHe75, NCoA-2, SRC2, Glucocorticoid Receptor-Interacting Protein-1, P160 Steroid Receptor Coactivator 2, EC 2.3.1.48, BHLHE75, KAT13C, GRIP1, and HTIF2. Canis lupus familiaris (canine) TIF-2 is encoded by the gene having an Ensembl identification number of ENSCAFG00000007775.

[0064] RAR is also referred to as: Retinoic Acid Receptor Alpha, RARA, Nuclear Receptor Subfamily 1 Group B Member 1, RAR-Alpha, NR1B1, Nucleophosmin-Retinoic Acid Receptor Alpha Fusion Protein NPM-RAR Long Form, Retinoic Acid Nuclear Receptor Alpha Variant, Retinoic Acid Nuclear Receptor Alpha Variant 2, Retinoic Acid Receptor, Alpha Polypeptide, and Retinoic Acid Receptor, Alpha. Canis lupus familiaris (canine) RAR is encoded by the gene having an Ensembl identification number of ENSCAFG00000016060.

[0065] BCL-6 is also referred to as: BCL6 Transcription Repressor, Zinc Finger Protein 51, Zinc Finger And BTB Domain-Containing Protein 27, BCL6, Transcription Repressor, B-Cell Lymphoma 6 Protein, B-Cell Lymphoma 5 Protein, B Cell CLL/Lymphoma 6, Protein LAZ, ZBTB27, ZNF51 BCL5, LAZ3, Lymphoma-Associated Zinc Finger Gene On Chromosome 3, Cys-His2 Zinc Finger Transcription Factor, Zinc Finger Transcription Factor BCL6S, B-Cell Lymphoma 6 Protein Transcript, and BCL6A. Canis lupus familiaris (canine) BCL-6 is encoded by the gene having an Ensembl identification number of ENSCAFG00000013904.

[0066] AML1 is also referred to as RUNX1, RUNX Family Transcription Factor 1, Runt-Related Transcription Factor 1, Runt Related Transcription Factor 1, Polyomavirus Enhancer-Binding Protein 2 Alpha B Subunit, SL3/AKV Core-Binding Factor Alpha B Subunit, SL3-3 Enhancer Factor 1 Alpha B Subunit, Acute Myeloid Leukemia 1 Protein, Oncogene AML-1, PEBP2-Alpha B, PEA2-Alpha B, and CBFA2. Canis lupus familiaris (canine) AML1 is encoded by the gene having an Ensembl identification number of ENSCAFG00000009596.

[0067] STAT5 is also referred to as STAT5A, Signal Transducer And Activator Of Transcription 5A, Epididymis Secretory Sperm Binding Protein, and MGF. Canis lupus familiaris (canine) STAT5 is encoded by the gene having an Ensembl identification number of ENSCAFG00000015346.

[0068] HDAC1 is also referred to as Histone Deacetylase 1, EC 3.5.1.98, RPD3L1, HD1, Reduced Potassium Dependency, Yeast Homolog-Like 1, GON-10, KDAC1, and RPD3. Canis lupus familiaris (canine) HDAC1 is encoded by the gene having an Ensembl identification number of ENSCAFG00000010597.

[0069] MYC is also referred to as MYC Proto-Oncogene, BHLH Transcription Factor, V-Myc Avian Myelocytomatosis Viral Oncogene Homolog, Class E Basic Helix-Loop-Helix Protein 39, Myc Proto-Oncogene Protein, Transcription Factor P64, Proto-Oncogene C-Myc, BHLHe39, Myc-Related Translation/Localization Regulatory Factor, Avian Myelocytomatosis Viral Oncogene Homolog, V-Myc Myelocytomatosis Viral Oncogene Homolog, C-Myc, MRTL, and MYCC. Canis lupus familiaris (canine) MYC is encoded by the gene having an Ensembl identification number of ENSCAFG00000001086.

[0070] ALK is also referred to as ALK Receptor Tyrosine Kinase, Anaplastic Lymphoma Receptor Tyrosine Kinase, and ALK Tyrosine Kinase Receptor. Canis lupus familiaris (canine) ALK is encoded by the gene having an Ensembl identification number ENSCAFG00000005297.

[0071] c-MET is also referred to as MET Proto-Oncogene, Receptor Tyrosine Kinase, Hepatocyte Growth Factor Receptor, Tyrosine-Protein Kinase Met, Scatter Factor Receptor, Proto-Oncogene C-Met, HGF/SF Receptor, HGF Receptor, and SF Receptor. Canis lupus familiaris (canine) c-MET is encoded by the gene having an Ensembl identification number ENSCAFG00000003406.

[0072] ROS1 is also referred to as ROS Proto-Oncogene 1, Receptor Tyrosine Kinase, V-Ros Avian UR2 Sarcoma Virus Oncogene Homolog 1, C-Ros Oncogene 1 , Receptor Tyrosine Kinase, Proto-Oncogene Tyrosine-Protein Kinase ROS, and Proto-Oncogene C-Ros-1. Canis lupus familiaris (canine) ROS1 is encoded by the gene having an Ensembl identification number ENSCAFG00000000923.

[0073] As used herein, the term "VEGFRs" refers to the Vascular Endothelial Growth Factor Receptors, including (VEGFR-1, VEGFR-2, VEGFR-3).

[0074] VEGFR-1 is also referred to as Flt-1, Fms Related Tyrosine Kinase 1, Vascular Endothelial Growth Factor Receptor 1, Vascular Permeability Factor Receptor, Fms-Related Tyrosine Kinase 1 (Vascular Endothelial Growth Factor/Vascular Permeability Factor Receptor), Tyrosine-Protein Kinase Receptor FLT, Tyrosine-Protein Kinase FRT, and Fms-Like Tyrosine Kinase 1. Canis lupus familiaris (canine) VEGFR-1 is encoded by the gene having an Ensembl identification number ENSCAFG00000006701.

[0075] VEGFR-2 is also referred to as KDR, Flk-1, Kinase Insert Domain Receptor, Vascular Endothelial Growth Factor Receptor 2, Kinase Insert Domain Receptor (A Type III Receptor Tyrosine Kinase), Protein-Tyrosine Kinase Receptor Flk-1, Fetal Liver Kinase 1, Soluble VEGFR2 · CD309 Antigen, EC 2.7.10, VEGFR-2 or CD309. Canis lupus familiaris (canine) VEGFR-2 is encoded by the gene having an Ensembl identification number ENSCAFG00000002079.

[0076] VEGFR-3 is also referred to as Flt-4, Fms Related Tyrosine Kinase 4, Vascular Endothelial Growth Factor Receptor 3, Tyrosine-Protein Kinase Receptor FLT4, Fms-Like Tyrosine Kinase 4, EC 2.7.10.1, VEGFR3, Fms-Related Tyrosine Kinase 4, EC 2.7.10, LMPH1A, LMPHM1, FLT41 or PCL. Canis lupus familiaris (canine) VEGFR-3 is encoded by the gene having an Ensembl identification number ENSCAFG00000000482.

[0077] RAF, as used herein, includes Raf family members: ARAF, BRAF, mutant BRAF V600E, and CRAF.

[0078] ARAF is also referred to as A-Raf Proto-Oncogene, Serine/Threonine Kinase, V-Raf Murine Sarcoma 3611 Viral Oncogene Homolog 1, Serine/Threonine-Protein Kinase A-Raf,

Proto-Oncogene A-Raf-1, Proto-Oncogene Pks, EC 2.7.11.1, ARAF1, PKS2, V-Raf Murine Sarcoma 3611 Viral Oncogene-Like Protein A-Raf Proto-Oncogene Serine/Threonine-Protein Kinase. Ras-Binding Protein DA-Raf, Proto-Oncogene A-Raf, Oncogene ARAF1, EC 2.7.11, A-RAF, RAFA1, or PKS. Canis lupus familiaris (canine) ARAF is encoded by the gene having an Ensembl identification number ENSCAFG00000015115.

[0079] BRAF is also referred to as B-Raf Proto-Oncogene, Serine/Threonine Kinase, V-Raf Murine Sarcoma Viral Oncogene Homolog B1, V-Raf Murine Sarcoma Viral Oncogene Homolog B, Serine/Threonine-Protein Kinase B-Raf, Proto-Oncogene B-Raf, BRAF1, RAFB1 B-Raf Serine/Threonine-Protein, 94 KDa B-Raf Protein, EC 2.7.11.1, B-RAF1, B-Raf, NS7, or P94. Canis lupus familiaris (canine) B-RAF is encoded by the gene having an Ensembl identification number ENSCAFG00000003907.

[0080] CRAF is also referred to as Raf-1, Raf-1 Proto-Oncogene, Serine/Threonine Kinase, RAF Proto-Oncogene Serine/Threonine-Protein Kinase, V-Raf-1 Murine Leukemia Viral Oncogene Homolog 1, C-Raf Proto-Oncogene, Serine/Threonine Kinase, Proto-Oncogene C-RAF, EC 2.7.11.1, Raf-1, V-Raf-1 Murine Leukemia Viral Oncogene-Like Protein 1, Raf Proto-Oncogene Serine/Threonine Protein Kinase Oncogene RAF1, EC 2.7.11, CMD1NN, C-Raf, CRAF. CRaf, NS5, or RAF. Canis lupus familiaris (canine) CRAF is encoded by the gene having an Ensembl identification number ENSCAFG00000004951.

[0081] FLT-3 is also referred to as Fms Related Tyrosine Kinase 3, Receptor-Type Tyrosine-Protein Kinase FLT3, Stem Cell Tyrosine Kinase 1, Fms-Like Tyrosine Kinase 3, FL Cytokine Receptor, CD135 Antigen, EC 2.7.10.1, CD135, FLK-2, FLK2, STK1, Growth Factor Receptor Tyrosine Kinase Type III, Fms-Related Tyrosine Kinase 3, Fetal Liver Kinase 2, Fetal Liver Kinase-2, EC 2.7.10, FLT-3, or STK-1. Canis lupus familiaris (canine) FLT-3 is encoded by the gene having an Ensembl identification number of: ENSCAFG00000006716.

[0082] RET is also referred to as Ret Proto-Oncogene, Proto-Oncogene Tyrosine-Protein Kinase Receptor Ret, Cadherin-Related Family Member 16, Rearranged During Transfection, RET Receptor Tyrosine Kinase Cadherin Family Member 12, Proto-Oncogene C-Ret, EC 2.7.10.1, CDHF12, CDHR16, PTC, Ret Proto-Oncogene (Multiple Endocrine Neoplasia And Medullary Thyroid Carcinoma 1, Hirschsprung Disease), Multiple Endocrine Neoplasia And Medullary Thyroid Carcinoma 1, Hirschsprung Disease 1, EC 2.7.10, RET-ELE1, HSCR1, MEN2A, MEN2B, RET51, or MTC1. Canis lupus familiaris (canine) RET is encoded by the gene having an Ensembl identification number of: ENSCAFG00000007076.

[0083] PDGFRB is also referred to as Platelet Derived Growth Factor Receptor, Beta Platelet-Derived Growth Factor Receptor, Beta Polypeptide, Beta-Type Platelet-Derived Growth Factor Receptor, Platelet-Derived Growth Factor Receptor Beta, Platelet-Derived Growth Factor Receptor 1, CD140 Antigen-Like Family Member B, PDGF-R-Beta, EC 2.7.10.1, PDGFR-Beta, PDGFR-1, PDGFR1, PDGFR, Beta Platelet-Derived Growth Factor Receptor, Activated Tyrosine Kinase PDGFRB , CD140b Antigen, NDEL1-PDGFRB, EC 2.7.10, CD140B, IBGC4, JTK12, PENTT, IMF1, and KOGS. Canis lupus familiaris (canine) PDGFRB is encoded by the gene having an Ensembl identification number of: ENSCAFG00000018214.

[0084] It must be noted that, as used in the specification and the appended claims, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise.

[0085] For the sake of brevity, only certain ranges are explicitly disclosed herein. However, ranges from any lower limit may be combined with any upper limit to recite a range not explicitly recited, as well as, ranges from any lower limit may be combined with any other lower limit to recite a range not explicitly recited, in the same way, ranges from any upper limit may be combined with any other upper limit to recite a range not explicitly recited. Additionally, whenever a numerical range with a lower limit and an upper limit is disclosed, any number and any included range falling within the range are specifically disclosed. In particular, every range of values (of the form, "from about a to about b," or, equivalently, "from approximately a to b," or, equivalently, "from approximately a-b", or "a-b") disclosed herein is to be understood to set forth every number and range encompassed within the broader range of values even if not explicitly recited. Thus, every point or individual value may serve as its own lower or upper limit combined with any other point or individual value or any other lower or upper limit, to recite a range not explicitly recited.

Methods

[0086] Described herein are methods of treating canine cancers comprising administration of a therapeutically effective amount of a pharmaceutical composition comprising HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof.

Types of cancers

[0087] Canine cancers include, but are not limited to, solid tumors, leukemia, lymphocytic leukemia, lymphoma, sarcoma, soft tissue sarcoma, multiple myeloma, hemangiosarcoma,

histiocytic sarcoma, hepatocellular carcinoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, subungual squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, apocrine gland anal sac adenocarcinomas (AGASACA), lung cancer, pulmonary adenocarcinoma, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer. The methods and compositions described herein, also can be used on any other cancers, including cancers that are rare in canines.

Modes of administration

[0088] In certain embodiments, the pharmaceutical compositions comprising the compounds described herein are administered to a subject in need thereof by oral administration. The pharmaceutical compositions can be formulated for administration to subjects by a variety of routes, including orally, intranasally, by inhalation, intramuscularly, intraperitoneally, and parenterally, including intravenously or subcutaneously. Pharmaceutical compositions can be formulated in volumes and concentrations suitable for bolus administration, for continuous infusion, or for subcutaneous administration. Pharmaceutical compositions comprising anti-cancer agents may be administered by any preferred route of administration.

Dosing regimens

[0089] The compounds described herein can be administered in at any suitable dose. An individual dose of the compound can be any ranging from 0.01-200 mg/kg, inclusive. An individual dose of the compound can a be 1.0-100 mg/kg, 100-200 mg/kg, 1.0-10 mg/kg, 10-20 mg/kg, 20-30 mg/kg, 30-40 mg/kg, 40-50 mg/kg; 50-60 mg/kg, 70-80 mg/kg, 80-90 mg/kg, 90-100 mg/kg, 10-100 mg/kg, 100-150 mg/kg, 150-200 mg/kg, 20-50 mg/kg, 50-100 mg/kg, 1.0-20 mg/kg, 1.0-10 mg/kg, 1.0-5.0 mg/kg, 1.0-2.0 mg/kg, 5-10 mg/kg, 10-15 mg/kg, 15-20 mg/kg, 0.5-1.5 mg/kg, 0.5-1.0 mg/kg, 0.1-1.0 mg/kg, 0.1-0.2 mg/kg, 0.2-0.3 mg/kg, 0.3-0.4 mg/kg, 0.4-0.5 mg/kg, 0.5-0.6 mg/kg, 0.6-0.7 mg/kg, 0.7-0.8 mg/kg, 0.8-0.9 mg/kg, 0.9-1.0 mg/kg, 0.01-0.1 mg/kg, 0.01-0.02 mg/kg, 0.02-0.03 mg/kg, 0.03-0.04 mg/kg, 0.04-0.05 mg/kg, 0.05-0.06 mg/kg, 0.06-0.07 mg/kg, 0.07-0.08 mg/kg, 0.08-0.09 mg/kg, 0.09-0.1 mg/kg, 1.0-3.0 mg/kg, 1.1-1.2 mg/kg, 1.2-1.3 mg/kg, 1.3-1.4 mg/kg, 1.4-1.5 mg/kg, 1.5-1.6 mg/kg, 1.6-1.7 mg/kg, 1.7-1.8 mg/kg, 1.8-1.9 mg/kg, 1.9-2.0 mg/kg, 2.0-2.1 mg/kg, 2.1-2.2 mg/kg, 2.2-2.3 mg/kg, 2.3-2.4 mg/kg, 2.4-2.5 mg/kg, 2.5-2.6 mg/kg, 2.6-2.7 mg/kg, 2.7-2.8 mg/kg, 2.8-2.9 mg/kg, or 2.9-3.0 mg/kg, inclusive.

[0090] In a variety of embodiments, the pharmaceutical compositions described herein are administered for a period of 1 day to indefinitely, a period of 1 week to 6 months, a period of

3 months to 5 years, a period of 6 months to 1 or 2 years, or the like. Optionally, administration is repeated; for example, in certain embodiments, the pharmaceutical compositions described herein are administered once daily, twice daily, three times daily, four times daily, five times daily, every two days, every three days, every five days, once a week, once every two weeks, once a month, every other month, semi-annually, or annually. In certain embodiments, the pharmaceutical compositions described herein are administered at regular intervals over a period of several weeks, followed by a period of rest, during which no pharmaceutical composition described herein is administered. For example, in certain embodiments, pharmaceutical compositions comprising a compound described herein are administered for one, two, three, or more weeks, followed by one, two, three, or more weeks without pharmaceutical composition administration. The repeated administration can be at the repeated; for example, in certain embodiments, the pharmaceutical composition comprising a compound described herein is administered once daily, twice daily, three times daily, four times daily, five times daily, every two days, every three days, every five days, once a week, once every two weeks, once a month, every other month, semi-annually, or annually. In certain embodiments, the pharmaceutical composition comprising a compound is administered at regular intervals over a period of several weeks, followed by a period of rest, during which no the pharmaceutical composition comprising a compound is administered. For example, in certain embodiments, the pharmaceutical composition is administered for one, two, three, or more weeks, followed by one, two, three, or more weeks without administration of the pharmaceutical composition comprising the compound. The repeated administration can be at the same dose of a different dose.

[0091] In certain embodiments, Rapamycin is administered at a dose of 0.05-0.5 mg/kg/day. In certain embodiments, Rapamycin is administered at a dose of 0.1 mg/kg/day. In certain embodiments, Trametinib is administered at a dose of 0.01-0.1 mg/kg/day. In certain embodiments, Trametinib is administered at a dose of 0.02 mg/kg/day. In certain embodiments, Trametinib is administered at a dose of 0.01-0.05 mg/kg/day. In certain embodiments, Trametinib is administered at a dose of 0.02-0.03 mg/kg/day. In certain embodiments, Trametinib is administered at a dose of 0.02 mg/kg/day. In certain embodiments, Trametinib is administered at a dose of 0.03 mg/kg/day. In certain embodiments, Lapatinib is administered at a dose of 1-20 mg/kg/day. In certain embodiments, Lapatinib is administered at a dose of 5-10 mg/kg/day. In certain embodiments, Lapatinib is administered at a dose of 5 mg/kg/day. In certain embodiments,

Lapatinib is administered at a dose of 6 mg/kg/day. In certain embodiments, Lapatinib is administered at a dose of 7 mg/kg/day. In certain embodiments, Lapatinib is administered at a dose of 8 mg/kg/day. In certain embodiments, Lapatinib is administered at a dose of 9 mg/kg/day. In certain embodiments, Lapatinib is administered at a dose of 10 mg/kg/day. In certain embodiments, Dasatinib is administered at a dose of 0.1-1.0 mg/kg/day. In certain embodiments, Dasatinib is administered at a dose of 0.5-0.7 mg/kg/day. In certain embodiments, Dasatinib is administered at a dose of 0.5 mg/kg/day. In certain embodiments, Dasatinib is administered at a dose of 0.6 mg/kg/day. In certain embodiments, Dasatinib is administered at a dose of 0.7 mg/kg/day. In certain embodiments, Vorinostat is administered at a dose 10-100 mg/kg/every other day. In certain embodiments, Vorinostat is administered at a dose 30-60 mg/kg/every other day. In certain embodiments, Vorinostat is administered at a dose 45 mg/kg/every other day. In certain embodiments, Imatinib is administered at a dose 1-100 mg/kg/day. In certain embodiments, Imatinib is administered at a dose of 10 mg/kg/day. In certain embodiments, Crizotinib is administered at a dose of 0.5-5.0 mg/kg/day. In certain embodiments, Crizotinib is administered at a dose of 1 mg/kg/day-2 mg/kg/day. In certain embodiments, Crizotinib is administered at a dose of 1 mg/kg/day. In certain embodiments, Sorafinib is administered at a dose of 0.5-5.0 mg/kg/day. In certain embodiments, Sorafinib is administered at a dose of 1 mg/kg/day-3 mg/kg/day. In certain embodiments, Sorafinib is administered at a dose of 1 mg/kg/day. In certain embodiments, Sorafinib is administered at a dose of 2 mg/kg/day. In certain embodiments, Sorafinib is administered at a dose of 3 mg/kg/day. In certain embodiments, Sorafinib is administered at a dose of 3 mg/kg/every other day. In certain embodiments, Sorafinib is administered at a dose of 3 mg/kg/week.

[0092] In certain embodiments, the subject has transitional cell carcinoma, and the subject is treated with Lapatinib. In certain embodiments, the subject has transitional cell carcinoma and the subject is treated with Lapatinib at a dose of 5-10 mg/kg/day. In certain embodiments, the subject has transitional cell carcinoma, and the subject is treated with Trametinib. In certain embodiments, the subject has transitional cell carcinoma, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day.

[0093] In certain embodiments, the subject has thyroid cancer, and the subject is treated with Lapatinib. In certain embodiments, the subject has thyroid cancer, and the subject is treated with Lapatinib at a dose of 5-10 mg/kg/day. In certain embodiments, the subject has thyroid cancer, and the subject is treated with Trametinib. In certain embodiments, the subject has

thyroid cancer, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day. In certain embodiments, the subject has thyroid cancer, and the subject is treated with Rapamycin. In certain embodiments, the subject has thyroid cancer, and the subject is treated with Rapamycin at a dose of 0.05-2 mg/kg/day. In certain embodiments, the subject has thyroid cancer, and the subject is treated with Rapamycin at a dose of 0.1 mg/kg/day.

[0094] In certain embodiments, the subject has squamous cell carcinoma, and the subject is treated with Lapatinib. In certain embodiments, the subject has squamous cell carcinoma, and the subject is treated with Lapatinib at a dose of 5-10 mg/kg/day. In certain embodiments, the subject has squamous cell carcinoma, and the subject is treated with Trametinib. In certain embodiments, the subject has squamous cell carcinoma, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day.

[0095] In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Trametinib. In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day. In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Rapamycin. In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Rapamycin at a dose of 0.05-2 mg/kg/day. In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Rapamycin at a dose of 0.1 mg/kg/day. In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Dasatinib. In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Dasatinib at a dose of 0.1-1.0 mg/kg/day. In certain embodiments, the subject has soft tissue sarcoma, and the subject is treated with Dasatinib at a dose of 0.5-0.7 mg/kg/day.

[0096] In certain embodiments, the subject has pulmonary adenocarcinoma, and the subject is treated with Lapatinib. In certain embodiments, the subject has pulmonary adenocarcinoma and the subject is treated with Lapatinib at a dose of 5-10 mg/kg/day. In certain embodiments, the subject has pulmonary adenocarcinoma, and the subject is treated with Trametinib. In certain embodiments, the subject has pulmonary adenocarcinoma, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day.

[0097] In certain embodiments, the subject has osteosarcoma, and the subject is treated with Rapamycin. In certain embodiments, the subject has osteosarcoma, and the subject is treated with Rapamycin at a dose of 0.05-2 mg/kg/day. In certain embodiments, the subject has osteosarcoma, and the subject is treated with Rapamycin at a dose of 0.1 mg/kg/day. In certain embodiments, the subject has osteosarcoma, and the subject is treated with Dasatinib.

In certain embodiments, the subject has osteosarcoma, and the subject is treated with Dasatinib at a dose of 0.1-1.0 mg/kg/day. In certain embodiments, the subject has osteosarcoma, and the subject is treated with Dasatinib at a dose of 0.5-0.7 mg/kg/day.

[0098] In certain embodiments, the subject has melanoma, and the subject is treated with Rapamycin. In certain embodiments, the subject has melanoma, and the subject is treated with Rapamycin at a dose of 0.05-2 mg/kg/day. In certain embodiments, the subject has melanoma, and the subject is treated with Rapamycin at a dose of 0.1 mg/kg/day. In certain embodiments, the subject has melanoma, and the subject is treated with Dasatinib. In certain embodiments, the subject has melanoma, and the subject is treated with Dasatinib at a dose of 0.1-1.0 mg/kg/day. In certain embodiments, the subject has melanoma, and the subject is treated with Dasatinib at a dose of 0.5-0.7 mg/kg/day. In certain embodiments, the subject has melanoma, and the subject is treated with Trametinib. In certain embodiments, the subject has melanoma, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day.

[0099] In certain embodiments, the subject has mast cell tumor(s), and the subject is treated with Imatinib. In certain embodiments, the subject has mast cell tumor(s), and the subject is treated with Imatinib at a dose of 1-20 mg/kg/day. In certain embodiments, the subject has mast cell tumor(s), and the subject is treated with Imatinib at a dose of 10 mg/kg/day.

[00100] In certain embodiments, the subject has histocytic sarcoma, and the subject is treated with Trametinib. In certain embodiments, the subject has histocytic sarcoma, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day. In certain embodiments, the subject has histocytic sarcoma, and the subject is treated with Vorinostat. In certain embodiments, the subject has histocytic sarcoma, and the subject is treated with Vorinostat at a dose of 10-50 mg/kg/day. In certain embodiments, the subject has histocytic sarcoma, and the subject is treated with Vorinostat at a dose of 30 mg/kg/day.

[00101] In certain embodiments, the subject has hepatocellular carcinoma, and the subject is treated with Vorinostat. In certain embodiments, the subject has hepatocellular carcinoma, and the subject is treated with Vorinostat at a dose of 10-50 mg/kg/day. In certain embodiments, the subject has hepatocellular carcinoma, and the subject is treated with Vorinostat at a dose of 30 mg/kg/day. In certain embodiments, the subject has hepatocellular carcinoma, and the subject is treated with Rapamycin. In certain embodiments, the subject has hepatocellular carcinoma, and the subject is treated with Rapamycin at a dose of 0.05-2 mg/kg/day. In certain embodiments, the subject has hepatocellular carcinoma, and the subject is treated with Rapamycin at a dose of 0.1 mg/kg/day.

[00102] . In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Rapamycin. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Rapamycin at a dose of 0.05-2 mg/kg/day. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Rapamycin at a dose of 0.1 mg/kg/day. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Vorinostat. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Vorinostat at a dose of 10-50 mg/kg/day. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Vorinostat at a dose of 30 mg/kg/day. . In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Dasatinib. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Dasatinib at a dose of 0.1-1.0 mg/kg/day. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Dasatinib at a dose of 0.5-0.7 mg/kg/day. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Trametinib. In certain embodiments, the subject has hemangiosarcoma, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day.

[00103] In certain embodiments, the subject has apocrine gland anal sac adenocarcinoma (AGASACA), and the subject is treated with Trametinib. In certain embodiments, the subject has AGASACA, and the subject is treated with Trametinib at a dose of 0.02-0.03 mg/kg/day. In certain embodiments, the subject has AGASACA, and the subject is treated with Lapatinib. In certain embodiments, the subject has AGASACA and the subject is treated with Lapatinib at a dose of 5-10 mg/kg/day.

Diagnostic assays

[00104] In certain embodiments, described herein are methods of identifying subjects with cancer that will respond to pharmaceutical compositions comprising a compound described herein. In various embodiments, described herein are methods of treating cancer in a canine subject comprising administration of pharmaceutical compositions comprising a compound described herein and further comprising the step of determining or having determined if the cancer harbors at least one mutation in one or more genes prior to the administration of the pharmaceutical composition comprising a compound described herein. In various embodiments, described herein are methods of treating cancer in a canine subject comprising administration of pharmaceutical compositions comprising a compound described herein and further comprising the step of determining or having determined if the cancer overexpresses or underexpresses one or more genes compared to non-cancerous tissue prior to the

administration of the pharmaceutical composition comprising a compound described herein.In certain embodiments, at least one mutation in at least one gene is ATM kinase, prior to the administration of a pharmaceutical composition comprising a HDAC inhibitor. In certain embodiments, at least one mutation in at least one gene is selected from the group consisting of mTOR, PI3K, AKT and Ras, prior to the administration of a pharmaceutical composition comprising Rapamycin. In certain embodiments, at least one mutation in at least one gene is a gene that regulates or is regulated by mTOR, PI3K, AKT and Ras. In certain embodiments, at least one mutation in at least one gene is selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase prior to the administration of a pharmaceutical composition comprising Dasatinib. In certain embodiments, at least one mutation in at least one gene is selected from the group consisting of ERBB1 and ERBB2 prior to the administration a pharmaceutical composition comprising Lapatinib. In certain embodiments, at least one mutation in at least one gene is selected from the group consisting of MEK1 and MEK2 prior to the administration of a pharmaceutical composition comprising Trametinib. In certain embodiments, at least one mutation in at least one gene is selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1 prior to the administration of a pharmaceutical composition comprising Vorinostat. In certain embodiments, at least one mutation in at least one gene is selected from the group consisting of ABL, BCR-ABL, PDGFR, and C-KIT prior to the administration of a pharmaceutical composition comprising Imatinib. In certain embodiments, at least one mutation in at least one gene is a gene that regulates or is regulated by of ALK, c-MET and ROS1 prior to the administration of a pharmaceutical composition comprising Crizotinib. In certain embodiments, at least one mutation in at least one gene is selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB prior to the administration of a pharmaceutical composition comprising Sorafenib. In certain embodiments, the determining at least one mutation in at least one gene is determined from a biological sample derived from the cancer. In certain embodiments, the biological sample comprises nucleic acid. The nucleic acid can be DNA, RNA or combinations thereof. Any method known in the art can be used to determine the sequence of a gene. In certain embodiments, the determining is performed by sequencing nucleic acid.

[00105] In certain aspects, the mutation is a splice variant, a frameshift, a missense, or a nonsense mutation. In certain aspects, the at least one mutation of at least one gene is shown in Tables 1, 2 or 12-26. In certain aspects, the at least one mutation is a mutation in the ATM

gene is shown in Table 2. In certain embodiments, the cancer harbors a mutation in one or more genes selected from a gene listed in Tables 1, 2 and 12-26. In certain embodiments, the cancer harbors a mutation in one or more genes selected from a gene listed in Tables 1, 2 and 12-26, the cancer is one listed in Tables 1,2 and 12-26 and the cancer is treated with a targeted drug listed in Tables 1,2 and 12-26.

[00106] In certain aspects, the at least one mutation is a mutation in BRAF. In certain aspects, the at least one mutation is a mutation in SETD2. In certain aspects, the at least one mutation is a mutation in PDGFRβ. In certain aspects, the at least one mutation is a mutation in Notch 1. In certain aspects, the at least one mutation is a mutation in p53. In certain aspects, the at least one mutation is a mutation in PIK3CA. In certain aspects, the at least one mutation is a mutation in PTEN.

[00107] In certain embodiments, the biological sample is derived from a subject with transitional cell carcinoma, it is determined that the cancer harbors a mutation in BRAF, and the subject is selected for treatment with Lapatinib, Trametinib or combinations thereof. In certain embodiments, the biological sample is derived from a subject with thyroid cancer, the cancer harbors a mutation in Notch1, and the subject is selected for treatment with Trametinib, Lapatinib, Rapamycin, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with squamous cell carcinoma, it is determined that the cancer harbors a mutation in PDGFRβ, and the subject is selected for treatment with Trametinib, Lapatinib, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with squamous cell carcinoma, it is determined that the cancer harbors a mutation in SETD2, and the subject is selected for treatment with Trametinib, Lapatinib, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with soft tissue sarcoma, it is determined that the cancer harbors a mutation in SETD2, and the subject is selected for treatment with trametinib, dasatinib, rapamycin, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with soft tissue sarcoma, it is determined that the cancer harbors a mutation in ATM, and the subject is selected for treatment with trametinib, dasatinib, rapamycin, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with has osteosarcoma, it is determined that the cancer harbors a mutation in SETD2, and the subject is selected for treatment with dasatinib, rapamycin, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with melanoma, it is determined that the cancer harbors a mutation in SETD2, and the

subject is selected for treatment with trametinib, dasatinib, rapamycin, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with mast cell tumor, it is determined that the cancer harbors a mutation in SETD2, and the subject is seclected for treatment with imatinib. In certain embodiments, the biological sample is derived from a subject with mast cell tumor, it is determined that the cancer harbors a mutation in PDGFRβ, and the subject is selected for treatment with imatinib. In certain embodiments, the biological sample is derived from a subject with mast cell tumor, it is determined that the cancer harbors a mutation in Notch1, and the subject is selected for treatment with imatinib. In certain embodiments, the biological sample is derived from a subject with hemangiosarcoma sarcoma, it is determined that the cancer harbors a mutation in PIK3CA, and the subject is selected for treatment with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with hemangiosarcoma sarcoma, it is determined that the cancer harbors a mutation in p53, and the subject is selected for treatment with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with hemangiosarcoma sarcoma, it is determined that the cancer harbors a mutation in PTEN, and the subject is selected for treatment with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the biological sample is derived from a subject with hemangiosarcoma, it is determined that the cancer harbors a mutation in Notch1, and the subject is selected for treatment with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof.

[00108] In certain embodiments, the subject has transitional cell carcinoma, the cancer harbors a mutation in BRAF and the subject is treated with Lapatinib, Trametinib or combinations thereof. In certain embodiments, the subject has thyroid cancer, the cancer harbors a mutation in Notch1, and the subject is treated with Trametinib, Lapatinib, Rapamycin, or combinations thereof. In certain embodiments, the subject has squamous cell carcinoma, the cancer harbors a mutation in PDGFRβ, and the subject is treated with Trametinib, Lapatinib, or combinations thereof. In certain embodiments, the subject has squamous cell carcinoma, the cancer harbors a mutation in SETD2, and the subject is treated with Trametinib, Lapatinib, or combinations thereof. In certain embodiments, the subject has soft tissue sarcoma, the cancer harbors a mutation in SETD2, and the subject is treated with trametinib, dasatinib, rapamycin, or combinations thereof. In certain embodiments, the subject has soft tissue sarcoma, the cancer harbors a mutation in ATM, and the subject is

treated with trametinib, dasatinib, rapamycin, or combinations thereof. In certain embodiments, the subject has osteosarcoma, the cancer harbors a mutation in SETD2, and the subject is treated with dasatinib, rapamycin, or combinations thereof. In certain embodiments, the subject has melanoma, the cancer harbors a mutation in SETD2, and the subject is treated with trametinib, dasatinib, rapamycin, or combinations thereof. In certain embodiments, the subject has mast cell tumor, the cancer harbors a mutation in SETD2, and the subject is treated with imatinib. In certain embodiments, the subject has mast cell tumor, the cancer harbors a mutation in PDGFRβ, and the subject is treated with imatinib. In certain embodiments, the subject has mast cell tumor, the cancer harbors a mutation in Notch1, and the subject is treated with imatinib. In certain embodiments, the subject has hemangiosarcoma sarcoma, the cancer harbor a mutation in PIK3CA, and the subject is treated with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the subject has hemangiosarcoma sarcoma, the cancer harbor a mutation in p53, and the subject is treated with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the subject has hemangiosarcoma sarcoma, the cancer harbor a mutation in PTEN, and the subject is treated with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the subject has hemangiosarcoma sarcoma, the cancer harbor a mutation in Notch1, and the subject is treated with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof.

[00109] In certain embodiments, the determining if the cancer overexpresses or underexpresses one or more genes compared to non-cancerous tissue prior to the administration of the pharmaceutical composition is determined from a biological sample derived from the cancer. In certain embodiments, the biological sample comprises nucleic acid. The nucleic acid can be DNA, RNA or combinations thereof. Any method known in the art can be used to determine the expression of a gene, such as, but not limited to, immunohistochemistry, quantitative PCR and RNA-Seq. In certain embodiments, the one or more genes overexpressed or underexpressed in the cancer is a gene listed in Tables 1, and 12-26. In certain embodiments, the cancer overexpresses or underexpresses one or more genes compared to non-cancerous tissue selected from a gene listed in Tables 1, and 12-26. In certain embodiments, the cancer overexpresses or underexpresses one or more genes compared to non-cancerous tissue selected from a gene listed in Tables 1, and 12-26, the

cancer is one listed in Tables 1, and 12-26, and the cancer is treated with a targeted drug listed in Tables 1 and 12-26.

[00110] In certain embodiments, the cancer is Transitional Cell Carcinoma and the gene that is overexpressed is ERBB2. In certain embodiments, the cancer is Transitional Cell Carcinoma, the gene that is overexpressed is ERBB2, and the cancer harbors a mutation in BRAF. In certain embodiments, the cancer is Transitional Cell Carcinoma, the gene that is overexpressed is ERBB2, and the subject is treated with Lapatinib, Trametinib, or combinations thereof. In certain embodiments, the cancer is Transitional Cell Carcinoma, the gene that is overexpressed is ERBB2, the cancer harbors a mutation in BRAF, and the subject is treated with Lapatinib, Trametinib, or combinations thereof.

[00111] In certain embodiments, the cancer is Thyroid Carcinoma and the gene that is overexpressed is one or more genes shown in Table 13. In certain embodiments, the cancer is Thyroid Carcinoma, the gene that is overexpressed is one or more genes shown in Table 13, and the cancer harbors a mutation in one or more genes shown in Table 13. In certain embodiments, the cancer is Thyroid Carcinoma, the gene that is overexpressed is one or more genes shown in Table 13, the cancer harbors a mutation in one or more genes shown in Table 13, and the subject is treated with Lapatinib, Trametinib, Rapamycin or combinations thereof.

[00112] In certain embodiments, the cancer is Squamous Cell Carcinoma and the gene that is overexpressed is one or more genes shown in Table 15. In certain embodiments, the cancer is Squamous Cell Carcinoma, the gene that is overexpressed is one or more genes shown in Table 15, and the cancer harbors a mutation in one or more genes shown in Table 15. In certain embodiments, the cancer is Squamous Cell Carcinoma, the gene that is overexpressed is one or more genes shown in Table 15, the cancer harbors a mutation in one or more genes shown in Table 15, and the subject is treated with Lapatinib, Trametinib, or combinations thereof. In certain embodiments, the cancer is Squamous Cell Carcinoma, the gene that is overexpressed is PDGFRβ or SETD2, the cancer harbors a mutation in PDGFRβ or SETD2, and the subject is treated with Lapatinib, Trametinib, or combinations thereof.

[00113] In certain embodiments, the cancer is Soft Tissue Sarcoma, and the gene that is overexpressed is one or more genes shown in Table 16. In certain embodiments, the cancer is Soft Tissue Sarcoma, the gene that is overexpressed is one or more genes shown in Table 16, and the cancer harbors a mutation in one or more genes shown in Table 16. In certain embodiments, the cancer is Soft Tissue Sarcoma, the gene that is overexpressed is one or more genes shown in Table 16, the cancer harbors a mutation in one or more genes shown in

Table 16, and the subject is treated with Rapamycin, Dasatinib, Trametinib, or combinations thereof. In certain embodiments, the cancer is Soft Tissue Sarcoma, the gene that is overexpressed is one or more genes shown in Table 16, the cancer harbors a mutation in ATM or SETD2, and the subject is treated with Rapamycin, Dasatinib Trametinib, or combinations thereof.

[00114] In certain embodiments, the cancer is Pulmonary Adenocarcinoma, and the gene that is overexpressed is one or more genes shown in Table 17. In certain embodiments, the cancer is Pulmonary Adenocarcinoma, the gene that is overexpressed is one or more genes shown in Table 17, and the cancer harbors a mutation in one or more genes shown in Table 17. In certain embodiments, the cancer is Pulmonary Adenocarcinoma, the gene that is overexpressed is one or more genes shown in Table 17, the cancer harbors a mutation in one or more genes shown in Table 17, and the subject is treated with Lapatinib, Trametinib, or combinations thereof. In certain embodiments, the cancer is Pulmonary Adenocarcinoma, the gene that is overexpressed is one or more genes shown in Table 17, the cancer harbors a mutation in Table 17, and the subject is treated with Lapatinib, Trametinib, or combinations thereof.

[00115] In certain embodiments, the cancer is Osteosarcoma, and the gene that is overexpressed is one or more genes shown in Table 18. In certain embodiments, the cancer is Osteosarcoma, the gene that is overexpressed is one or more genes shown in Table 18, and the cancer harbors a mutation in one or more genes shown in Table 18. In certain embodiments, the cancer is Osteosarcoma, the gene that is overexpressed is one or more genes shown in Table 18, and the cancer harbors a mutation in SETD2. In certain embodiments, the cancer is Osteosarcoma, the gene that is overexpressed is one or more genes shown in Table 18, the cancer harbors a mutation in one or more genes shown in Table 18, and the subject is treated with Dasatinib, Rapamycin, or combinations thereof. In certain embodiments, the cancer is Osteosarcoma, the gene that is overexpressed is one or more genes shown in Table 18, the cancer harbors a mutation in Table 18, and the subject is treated with Dasatinib, Rapamycin, or combinations thereof. In certain embodiments, the cancer is Osteosarcoma, the gene that is overexpressed is one or more genes shown in SETD2, the cancer harbors a mutation in Table 18, and the subject is treated with Dasatinib, Rapamycin, or combinations thereof.

[00116] In certain embodiments, the cancer is Melanoma, and the gene that is overexpressed is one or more genes shown in Table 19. In certain embodiments, the cancer is

Melanoma, the gene that is overexpressed is one or more genes shown in Table 19, and the cancer harbors a mutation in one or more genes shown in Table 19. In certain embodiments, the cancer is Melanoma, the gene that is overexpressed is one or more genes shown in Table 19, and the cancer harbors a mutation in SETD2. In certain embodiments, the cancer is Melanoma, the gene that is overexpressed is one or more genes shown in Table 19, the cancer harbors a mutation in one or more genes shown in Table 19, and the subject is treated with Dasatinib, Rapamycin, Trametinib or combinations thereof. In certain embodiments, the cancer is Melanoma, the gene that is overexpressed is one or more genes shown in Table 19, the cancer harbors a mutation in Table 19, and the subject is treated with Dasatinib, Rapamycin, Trametinib or combinations thereof. In certain embodiments, the cancer is Melanoma, the gene that is overexpressed is one or more genes shown in SETD2, the cancer harbors a mutation in Table 19, and the subject is treated with Dasatinib, Rapamycin, Trametinib or combinations thereof.

[00117] In certain embodiments, the cancer is Mast Cell Tumor, and the gene that is overexpressed is one or more genes shown in Table 20. In certain embodiments, the cancer is Mast Cell Tumor, the gene that is overexpressed is one or more genes shown in Table 20, and the cancer harbors a mutation in one or more genes shown in Table 20. In certain embodiments, the cancer is Mast Cell Tumor, the gene that is overexpressed is one or more genes shown in Table 20, and the cancer harbors a mutation in SETD2, PDGFRβ, Notch1, or combinations thereof. In certain embodiments, the cancer is Mast Cell Tumor, the gene that is overexpressed is one or more genes shown in Table 20, the cancer harbors a mutation in one or more genes shown in Table 20, and the subject is treated with Imatinib. In certain embodiments, the cancer is Mast Cell Tumor, the gene that is overexpressed is SETD2, PDGFRβ, Notch1, or combinations thereof, the cancer harbors a mutation in SETD2, PDGFRβ, Notch1, or combinations thereof, and the subject is treated with Imatinib. In certain embodiments, the cancer is Mast Cell Tumor, the gene that is overexpressed is one or more genes shown in Table 18, the cancer harbors a mutation in Table 20, and the subject is treated with Imatinib. In certain embodiments, the cancer is Mast Cell Tumor, the gene that is overexpressed is one or more genes shown in SETD2, PDGFRβ, Notch1, or combinations thereof the cancer harbors a mutation in Table 20, and the subject is treated with Imatinib.

[00118] In certain embodiments, the cancer is Histiocytic Sarcoma, and the gene that is overexpressed is one or more genes shown in Table 23. In certain embodiments, the cancer is Histiocytic Sarcoma, the gene that is overexpressed is one or more genes shown in Table 23,

and the cancer harbors a mutation in one or more genes shown in Table 23. In certain embodiments, the cancer is Histiocytic Sarcoma, the gene that is overexpressed is one or more genes shown in Table 23, the cancer harbors a mutation in one or more genes shown in Table 23, and the subject is treated with Vorinostat, Trametinib, or combinations thereof. In certain embodiments, the cancer is Histiocytic Sarcoma, the gene that is overexpressed is one or more genes shown in Table 23, the cancer harbors a mutation in Table 23, and the subject is treated with Vorinostat, Trametinib, or combinations thereof.

[00119] In certain embodiments, the cancer is Hepatocellular Carcinoma, and the gene that is overexpressed is one or more genes shown in Table 24. In certain embodiments, the cancer is Hepatocellular Carcinoma, the gene that is overexpressed is one or more genes shown in Table 24, and the cancer harbors a mutation in one or more genes shown in Table 24. In certain embodiments, the cancer is Hepatocellular Carcinoma, the gene that is overexpressed is one or more genes shown in Table 24, the cancer harbors a mutation in one or more genes shown in Table 24, and the subject is treated with Vorinostat, Rapamycin, or combinations thereof. In certain embodiments, the cancer is Hepatocellular Carcinoma, the gene that is overexpressed is one or more genes shown in Table 24, the cancer harbors a mutation in Table 24, and the subject is treated with Vorinostat, Rapamycin, or combinations thereof

[00120] In certain embodiments, the cancer is Hemangiosarcoma, and the gene that is overexpressed is one or more genes shown in Table 25. In certain embodiments, the cancer is Hemangiosarcoma, the gene that is overexpressed is one or more genes shown in Table 25, and the cancer harbors a mutation in one or more genes shown in Table 25. In certain embodiments, the cancer is Hemangiosarcoma, the gene that is overexpressed is one or more genes shown in Table 25, and the cancer harbors a mutation in PIK3CA, p53, PTEN, NOTCH1, or combinations thereof. In certain embodiments, the cancer is Hemangiosarcoma, the gene that is overexpressed is one or more genes shown in Table 25, the cancer harbors a mutation in one or more genes shown in Table 25, and the subject is treated with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the cancer is Hemangiosarcoma, the gene that is overexpressed is PIK3CA, p53, PTEN, NOTCH1, or combinations thereof, the cancer harbors a mutation in PIK3CA, p53, PTEN, NOTCH1, or combinations thereof, and the subject is treated with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the cancer is Hemangiosarcoma, the gene that is overexpressed is one or more genes shown in Table 18, the cancer harbors a mutation in Table 25, and the subject is treated with Rapamycin,

Trametinib, Dasatinib, Vorinostat, or combinations thereof. In certain embodiments, the cancer is Hemangiosarcoma, the gene that is overexpressed is one or more genes shown in PIK3CA, p53, PTEN, NOTCH1, or combinations thereof the cancer harbors a mutation in Table 25, and the subject is treated with Rapamycin, Trametinib, Dasatinib, Vorinostat, or combinations thereof.

[00121] In certain embodiments, the cancer is AGASACA, and the gene that is overexpressed is one or more genes shown in Table 26. In certain embodiments, the cancer is AGASACA, the gene that is overexpressed is one or more genes shown in Table 26, and the cancer harbors a mutation in one or more genes shown in Table 26. In certain embodiments, the cancer is AGASACA, the gene that is overexpressed is one or more genes shown in Table 26, the cancer harbors a mutation in one or more genes shown in Table 26, and the subject is treated with Lapatinib, Trametinib, or combinations thereof. In certain embodiments, the cancer is AGASACA, the gene that is overexpressed is one or more genes shown in Table 26, the cancer harbors a mutation in Table 26, and the subject is treated with Lapatinib, Trametinib, or combinations thereof.

Combination therapies

[00122] Administration of the pharmaceutical compositions described herein comprising a compound described herein can be concurrent with (at the same time), sequential to (at a different time but on the same day, e.g., during the same subject visit), or separate from (on a different day) administration of anther anti-cancer agent or therapy. When administered sequentially or separately, the pharmaceutical compositions comprising a compound described herein can be administered before, after, or both before and after the other anti-cancer agent or therapy. In certain embodiments, the additional therapy is surgery. In certain embodiments, the additional therapy is administration of ionizing radiation to the subject.

Compounds

[00123] The structure and methods of production of Rapamycin are known in the art. For example, methods of production of Rapamycin are described in United States Patent numbers 3,929,992 and 3,993,749 which are hereby incorporated by reference in their entirety. The structure of Rapamycin is described in Findlay et al in Can. J. of Chem 58, 579 (1980). In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Rapamycin that are known in the art.

[00124] The structure and methods of production of Dasatinib are known in the art. For example, the structure and methods of production of Dasatinib are described in United States

Patent numbers: 6,596,746; 7,491,725; 7,153,856; 7,125,875; and 8,680,103; which are hereby incorporated by reference in their entirety. In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Dasatinib.

[00125] The structure and methods of production of Lapatinib are known in the art. For example, the structure and methods of production of Lapatinib are described in United States Patent numbers: 6713485; 6727256; 7157466; 8513262; 8821927 which are hereby incorporated by reference in their entirety. In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Lapatinib that are known in the art.

[00126] The structure and methods of production of Trametinib are known in the art. For example, the structure and methods of production of Trametinib are described in United States Patent numbers: 7378423; 8580304; 8703781; 8835443; 8952018; 9155706; 9271941.

[00127] which are hereby incorporated by reference in their entirety. In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Trametinib that are known in the art.

[00128] The structure and methods of production of Vorinostat are known in the art. For example, the structure and methods of production of Vorinostat are described in United States Patent numbers: 7399787; 7456219; 7652069; 7732490; 7851509; 8067472; 8093295; 8101663; and 8450372, which are hereby incorporated by reference in their entirety. In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Vorinostat that are known in the art.

[00129] The structure and methods of production of Imatinib are known in the art. For example, the structure and methods of production of Imatinib are described in United States Patent numbers 6894051 and 6958335 which are hereby incorporated by reference in their entirety. In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Imatinib that are known in the art.

[00130] The structure and methods of production of Crizotinib are known in the art. For example, the structure and methods of production of Crizotinib are described in United States Patent numbers 7230098, 7825137, 7858643, 8217057, and 8785632 which are hereby incorporated by reference in their entirety. In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Crizotinib that are known in the art.

[00131] The structure and methods of production of Sorafenib are known in the art. For example, the structure and methods of production of Sorafenib are described in United States Patent numbers: 7235576, 7351834, 7897623, 8124630, 8618141, 8841330, 8877933, and 9737488 which are hereby incorporated by reference in their entirety. In certain embodiments, the pharmaceutical compositions described herein may also comprise derivatives of Sorafenib that are known in the art.

Anti-cancer agents

[00132] The pharmaceutical compositions described herein can be administered alone or in combination with other treatments, either simultaneously or sequentially dependent upon the condition to be treated. One or more additional anti-cancer agents may be administered to the subject. Anti-cancer agents can be, but are not limited to, chemotherapeutic agents, targeted therapies, hormones, and immunotherapies. Anti-cancer agents can be, but are not limited to, a small molecule, an antibody or antibody fragment, nucleic acid (e.g., DNA or RNA), carbohydrates, peptides, lipids, exosomes, cells, or combinations thereof. Chemotherapeutic agents include, but are not limited to alkylating agents, antimetabolites, anti-tumor antibiotics (e.g., doxorubicin, daunorubicin, bleomycin, dactinomycin), topoisomerase inhibitors (e.g., etoposide, irinotecan, topotecan), and mitotic inhibitors (e.g., docetaxel, eribulin, ixabepilone, paclitaxel, vinblastine). Examples of anti-cancer agents include, but are not limited to: Abemaciclib, Abiraterone Acetate, Abraxane (Paclitaxel Albumin-stabilized Nanoparticle Formulation), Acalabrutinib, Actemra (Tocilizumab), Adcetris (Brentuximab Vedotin), Ado-Trastuzumab Emtansine, Adriamycin (Doxorubicin Hydrochloride), Afatinib Dimaleate, Afinitor (Everolimus), Akynzeo (Netupitant and Palonosetron Hydrochloride), Aldara (Imiquimod), Aldesleukin, Alecensa (Alectinib), Alectinib, Alemtuzumab, Alimta (Pemetrexed Disodium), Aliqopa (Copanlisib Hydrochloride), Alkeran for Injection (Melphalan Hydrochloride), Alkeran Tablets (Melphalan), Aloxi (Palonosetron Hydrochloride), Alpelisib, Alunbrig (Brigatinib), Ameluz (Aminolevulinic Acid Hydrochloride), Amifostine, Aminolevulinic Acid Hydrochloride, Anastrozole, Apalutamide, Aprepitant, Aranesp (Darbepoetin Alfa), Aredia (Pamidronate Disodium), Arimidex (Anastrozole), Aromasin (Exemestane), Arranon (Nelarabine), Arsenic Trioxide, Arzerra (Ofatumumab), Asparaginase Erwinia chrysanthemi, Asparlas (Calaspargase Pegol-mknl), Atezolizumab, Avastin (Bevacizumab), Avelumab, Axicabtagene Ciloleucel, Axitinib, Azacitidine, Azedra (Iobenguane I 131), Balversa (Erdafitinib), Bavencio (Avelumab), Beleodaq (Belinostat), Belinostat, Bendamustine Hydrochloride, Bendeka (Bendamustine

Hydrochloride), Besponsa (Inotuzumab Ozogamicin), Bevacizumab, Bexarotene, Bicalutamide, BiCNU (Carmustine), Binimetinib, Bleomycin Sulfate, Blinatumomab, Blincyto (Blinatumomab), Bortezomib, Bosulif (Bosutinib), Bosutinib, Braftovi (Encorafenib), Brentuximab Vedotin, Brigatinib, BuMel, Busulfan, Busulfex (Busulfan), Cabazitaxel, Cablivi (Caplacizumab-yhdp), Cabometyx (Cabozantinib-S-Malate), Cabozantinib-S-Malate, Calaspargase Pegol-mknl, Calquence (Acalabrutinib), Campath (Alemtuzumab), Camptosar (Irinotecan Hydrochloride), Capecitabine, Caplacizumab-yhdp, Carac (Fluorouracil--Topical), Carboplatin, Carfilzomib, Carmustine, Carmustine Implant, Casodex (Bicalutamide), Cemiplimab-rwlc, Ceritinib, Cerubidine (Daunorubicin Hydrochloride), Cervarix (Recombinant HPV Bivalent Vaccine), Cetuximab, Chlorambucil, Cisplatin, Cladribine, Clofarabine, Clolar (Clofarabine), Cobimetinib, Cometriq (Cabozantinib-S-Malate), Copanlisib Hydrochloride, Copiktra (Duvelisib), Cosmegen (Dactinomycin), Cotellic (Cobimetinib), Crizotinib, Cyclophosphamide, Cyramza (Ramucirumab), Cytarabine, Cytarabine Liposome, Dabrafenib Mesylate, Dacarbazine, Dacogen (Decitabine), Dacomitinib, Dactinomycin, Daratumumab, Darbepoetin Alfa, Darzalex (Daratumumab), Dasatinib, Daunorubicin Hydrochloride, Daunorubicin Hydrochloride and Cytarabine Liposome, Daurismo (Glasdegib Maleate), Decitabine, Defibrotide Sodium, Defitelio (Defibrotide Sodium), Degarelix, Denileukin Diftitox, Denosumab, DepoCyt (Cytarabine Liposome), Dexamethasone, Dexrazoxane Hydrochloride, Dinutuximab, Docetaxel, Doxil (Doxorubicin Hydrochloride Liposome), Doxorubicin Hydrochloride, Doxorubicin Hydrochloride Liposome, Durvalumab, Duvelisib, Efudex (Fluorouracil--Topical), Eligard (Leuprolide Acetate), Elitek (Rasburicase), Ellence (Epirubicin Hydrochloride), Elotuzumab, Eloxatin (Oxaliplatin), Eltrombopag Olamine, Elzonris (Tagraxofusp-erzs), Emapalumab-lzsg, Emend (Aprepitant), Empliciti (Elotuzumab), Enasidenib Mesylate, Encorafenib, Enzalutamide, Epirubicin Hydrochloride, Epoetin Alfa, Epogen (Epoetin Alfa), Erbitux (Cetuximab), Erdafitinib, Eribulin Mesylate, Erivedge (Vismodegib), Erleada (Apalutamide), Erlotinib Hydrochloride, Erwinaze (Asparaginase Erwinia chrysanthemi), Ethyol (Amifostine) Etopophos (Etoposide Phosphate), Etoposide, Etoposide Phosphate, Everolimus Evista (Raloxifene Hydrochloride), Evomela (Melphalan Hydrochloride), Exemestane, 5-FU (Fluorouracil Injection), 5-FU (Fluorouracil--Topical), Fareston (Toremifene), Farydak (Panobinostat), Faslodex (Fulvestrant), Femara (Letrozole), Filgrastim, Firmagon (Degarelix), Fludarabine Phosphate, Fluoroplex (Fluorouracil--Topical), Fluorouracil Injection, Fluorouracil—Topical, Flutamide,

Folotyn (Pralatrexate), Fostamatinib Disodium, Fulvestrant, Fusilev (Leucovorin Calcium), Gamifant (Emapalumab-lzsg), Gardasil (Recombinant HPV Quadrivalent Vaccine), Gardasil 9 (Recombinant HPV Nonavalent Vaccine), Gazyva (Obinutuzumab), Gefitinib, Gemcitabine Hydrochloride, Gemtuzumab Ozogamicin, Gemzar (Gemcitabine Hydrochloride), Gilotrif (Afatinib Dimaleate), Gilteritinib Fumarate, Glasdegib Maleate, Gleevec (Imatinib Mesylate), Gliadel Wafer (Carmustine Implant), Glucarpidase, Goserelin Acetate, Granisetron, Granisetron Hydrochloride, Granix (Filgrastim), Halaven (Eribulin Mesylate), Hemangeol (Propranolol Hydrochloride), Herceptin Hylecta (Trastuzumab and Hyaluronidase-oysk), Herceptin (Trastuzumab), HPV Bivalent Vaccine, Recombinant, HPV Nonavalent Vaccine, Recombinant, HPV Quadrivalent Vaccine, Recombinant, Hycamtin (Topotecan Hydrochloride), Hydrea (Hydroxyurea), Hydroxyurea, Ibrance (Palbociclib), Ibritumomab Tiuxetan, Ibrutinib, Iclusig (Ponatinib Hydrochloride), Idamycin PFS (Idarubicin Hydrochloride), Idarubicin Hydrochloride, Idelalisib, Idhifa (Enasidenib Mesylate), Ifex (Ifosfamide), Ifosfamide, IL-2 (Aldesleukin), Imatinib Mesylate, Imbruvica (Ibrutinib), Imfinzi (Durvalumab), Imiquimod, Imlygic (Talimogene Laherparepvec), Inlyta (Axitinib), Inotuzumab Ozogamicin, Interferon Alfa-2b, Recombinant, Interleukin-2 (Aldesleukin), Intron A (Recombinant Interferon Alfa-2b), Iobenguane I 131, Ipilimumab, Iressa (Gefitinib), Irinotecan Hydrochloride, Irinotecan Hydrochloride Liposome, Istodax (Romidepsin), Ivosidenib, Ixabepilone, Ixazomib Citrate, Ixempra (Ixabepilone), Jakafi (Ruxolitinib Phosphate), Jevtana (Cabazitaxel), Kadcyla (Ado-Trastuzumab Emtansine), Kepivance (Palifermin), Keytruda (Pembrolizumab), Kisqali (Ribociclib), Kymriah (Tisagenlecleucel), Kyprolis (Carfilzomib), Lanreotide Acetate, Lapatinib Ditosylate, Larotrectinib Sulfate, Lartruvo (Olaratumab), Lenalidomide, Lenvatinib Mesylate, Lenvima (Lenvatinib Mesylate), Letrozole, Leucovorin Calcium, Leukeran (Chlorambucil), Leuprolide Acetate, Levulan Kerastik (Aminolevulinic Acid Hydrochloride), Libtayo (Cemiplimab-rwlc), Lomustine, Lonsurf (Trifluridine and Tipiracil Hydrochloride), Lorbrena (Lorlatinib), Lorlatinib, Lumoxiti (Moxetumomab Pasudotox-tdfk), Lupron (Leuprolide Acetate), Lupron Depot (Leuprolide Acetate), Lutathera (Lutetium Lu 177-Dotatate), Lutetium (Lu 177-Dotatate), Lynparza (Olaparib), Marqibo (Vincristine Sulfate Liposome), Matulane (Procarbazine Hydrochloride), Mechlorethamine Hydrochloride, Megestrol Acetate, Mekinist (Trametinib), Mektovi (Binimetinib), Melphalan, Melphalan Hydrochloride, Mercaptopurine, Mesna, Mesnex (Mesna), Methotrexate, Methylnaltrexone Bromide, Midostaurin, Mitomycin C, Mitoxantrone Hydrochloride, Mogamulizumab-kpkc, Moxetumomab Pasudotox-tdfk,

Mozobil (Plerixafor), Mustargen (Mechlorethamine Hydrochloride), Mvasi (Bevacizumab), Myleran (Busulfan), Mylotarg (Gemtuzumab Ozogamicin), Nanoparticle Paclitaxel (Paclitaxel Albumin-stabilized Nanoparticle Formulation), Navelbine (Vinorelbine Tartrate), Necitumumab, Nelarabine, Neratinib Maleate, Nerlynx (Neratinib Maleate), Netupitant and Palonosetron Hydrochloride, Neulasta (Pegfilgrastim), Neupogen (Filgrastim), Nexavar (Sorafenib Tosylate), Nilandron (Nilutamide), Nilotinib, Nilutamide, Ninlaro (Ixazomib Citrate), Niraparib Tosylate Monohydrate, Nivolumab, Nplate (Romiplostim), Obinutuzumab, Odomzo (Sonidegib), Ofatumumab, Olaparib, Olaratumab, Omacetaxine Mepesuccinate, Oncaspar (Pegaspargase), Ondansetron Hydrochloride, Onivyde (Irinotecan Hydrochloride Liposome), Ontak (Denileukin Diftitox), Opdivo (Nivolumab), Osimertinib Mesylate, Oxaliplatin, Paclitaxel, Paclitaxel Albumin-stabilized Nanoparticle Formulation Palbociclib, Palifermin, Palonosetron Hydrochloride, Palonosetron Hydrochloride and Netupitant, Pamidronate Disodium, Panitumumab, Panobinostat, Pazopanib Hydrochloride, Pegaspargase, Pegfilgrastim, Peginterferon Alfa-2b, PEG-Intron (Peginterferon Alfa-2b), Pembrolizumab, Pemetrexed Disodium, Perjeta (Pertuzumab), Pertuzumab, Piqray (Alpelisib), Plerixafor, Polatuzumab Vedotin-piiq, Polivy (Polatuzumab Vedotin-piiq), Pomalidomide, Pomalyst (Pomalidomide), Ponatinib Hydrochloride, Portrazza (Necitumumab), Poteligeo (Mogamulizumab-kpkc), Pralatrexate, Prednisone, Procarbazine Hydrochloride, Procrit (Epoetin Alfa), Proleukin (Aldesleukin), Prolia (Denosumab), Promacta (Eltrombopag Olamine), Propranolol Hydrochloride, Provenge (Sipuleucel-T), Purinethol (Mercaptopurine), Purixan (Mercaptopurine), Radium 223 Dichloride, Raloxifene Hydrochloride, Ramucirumab, Rasburicase, Ravulizumab-cwvz, Recombinant Human Papillomavirus (HPV) Bivalent Vaccine, Recombinant Human Papillomavirus (HPV) Nonavalent Vaccine, Recombinant Human Papillomavirus (HPV) Quadrivalent Vaccine, Recombinant Interferon Alfa-2b, Regorafenib, Relistor (Methylnaltrexone Bromide), Retacrit (Epoetin Alfa), Revlimid (Lenalidomide), Rheumatrex (Methotrexate), Ribociclib, Rituxan (Rituximab), Rituxan Hycela (Rituximab and Hyaluronidase Human), Rituximab, Rituximab and Hyaluronidase Human, Rolapitant Hydrochloride, Romidepsin, Romiplostim, Rubidomycin (Daunorubicin Hydrochloride), Rubraca (Rucaparib Camsylate), Rucaparib Camsylate, Ruxolitinib Phosphate, Rydapt (Midostaurin), Sancuso (Granisetron), Sclerosol Intrapleural Aerosol (Talc), Siltuximab, Sipuleucel-T, Somatuline Depot (Lanreotide Acetate), Sonidegib, Sorafenib Tosylate, Sprycel (Dasatinib), Sterile Talc Powder (Talc), Steritalc (Talc), Stivarga (Regorafenib), Sunitinib Malate, Sustol (Granisetron), Sutent

(Sunitinib Malate), Sylatron (Peginterferon Alfa-2b), Sylvant (Siltuximab), Synribo (Omacetaxine Mepesuccinate), Tabloid (Thioguanine), Tafinlar (Dabrafenib Mesylate), Tagraxofusp-erzs, Tagrisso (Osimertinib Mesylate), Talazoparib Tosylate, Talc, Talimogene Laherparepvec, Talzenna (Talazoparib Tosylate), Tamoxifen Citrate, Tarceva (Erlotinib Hydrochloride), Targretin (Bexarotene), Tasigna (Nilotinib), Tavalisse (Fostamatinib Disodium), Taxol (Paclitaxel), Taxotere (Docetaxel), Tecentriq (Atezolizumab), Temodar (Temozolomide), Temozolomide, Temsirolimus, Thalidomide, Thalomid (Thalidomide), Thioguanine, Thiotepa, Tibsovo (Ivosidenib), Tisagenlecleucel, Tocilizumab, Tolak (Fluorouracil--Topical), Topotecan Hydrochloride, Toremifene, Torisel (Temsirolimus), Totect (Dexrazoxane Hydrochloride), Trabectedin, Trametinib, Trastuzumab, Trastuzumab and Hyaluronidase-oysk, Treanda (Bendamustine Hydrochloride), Trexall (Methotrexate), Trifluridine and Tipiracil Hydrochloride, Trisenox (Arsenic Trioxide), Tykerb (Lapatinib Ditosylate), Ultomiris (Ravulizumab-cwvz), Unituxin (Dinutuximab), Uridine Triacetate, Valrubicin, Valstar (Valrubicin), Vandetanib,Varubi (Rolapitant Hydrochloride), Vectibix (Panitumumab), VeIP, Velcade (Bortezomib), Vemurafenib, Venclexta (Venetoclax), Venetoclax, Verzenio (Abemaciclib), Vidaza (Azacitidine), Vinblastine Sulfate, Vincristine Sulfate, Vincristine Sulfate Liposome, Vinorelbine Tartrate, Vismodegib, Vistogard (Uridine Triacetate), Vitrakvi (Larotrectinib Sulfate), Vizimpro (Dacomitinib), Voraxaze (Glucarpidase), Vorinostat, Votrient (Pazopanib Hydrochloride), Vyxeos (Daunorubicin Hydrochloride and Cytarabine Liposome), Xalkori (Crizotinib), Xeloda (Capecitabine), Xgeva (Denosumab), Xofigo (Radium 223 Dichloride), Xospata (Gilteritinib Fumarate), Xtandi (Enzalutamide), Yervoy (Ipilimumab), Yescarta (Axicabtagene Ciloleucel), Yondelis (Trabectedin), Zaltrap (Ziv-Aflibercept), Zarxio (Filgrastim), Zejula (Niraparib Tosylate Monohydrate), Zelboraf (Vemurafenib), Zevalin (Ibritumomab Tiuxetan), Zinecard (Dexrazoxane Hydrochloride), Ziv-Aflibercept, Zofran (Ondansetron Hydrochloride), Zoladex (Goserelin Acetate), Zoledronic Acid, Zolinza (Vorinostat), Zometa (Zoledronic Acid), Zydelig (Idelalisib), Zykadia (Ceritinib), Zytiga (Abiraterone Acetate), and derivatives thereof.

Pharmaceutical compositions

[00133] Methods for treatment of cancer and hyperproliferative diseases described herein include administering a therapeutically effective amount of a compound described herein. A compound described herein can be formulated in pharmaceutical compositions. Additionally, in certain embodiments, the subject is administered one or more additional pharmaceutical

compositions comprising one or more additional anti-cancer agents. These compositions can comprise, in addition to a compound described herein and/or anti-cancer agent, a pharmaceutically acceptable excipient, carrier, buffer, stabiliser or other materials well known to those skilled in the art. Such materials should be non-toxic and should not interfere with the efficacy of the active ingredient. The precise nature of the carrier or other material can depend on the route of administration, e.g., oral, intravenous, cutaneous or subcutaneous, nasal, intramuscular, intraperitoneal routes.

[00134] Pharmaceutical compositions for oral administration can be in tablet, capsule, powder or liquid form. A tablet can include a solid carrier such as gelatin or an adjuvant. Liquid pharmaceutical compositions generally include a liquid carrier such as water, petroleum, animal or vegetable oils, mineral oil or synthetic oil. Physiological saline solution, dextrose or other saccharide solution or glycols such as ethylene glycol, propylene glycol or polyethylene glycol can be included.

[00135] For intravenous, cutaneous or subcutaneous injection, or injection at the site of affliction, the active ingredient will be in the form of a parenterally acceptable aqueous solution which is pyrogen-free and has suitable pH, isotonicity and stability. Those of relevant skill in the art are well able to prepare suitable solutions using, for example, isotonic vehicles such as Sodium Chloride Injection, Ringer's Injection, Lactated Ringer's Injection. Preservatives, stabilisers, buffers, antioxidants and/or other additives can be included, as required.

[00136] The pharmaceutically useful compound according to the present invention that is to be given to an individual, administration is preferably in a “therapeutically effective amount” or “prophylactically effective amount”(as the case can be, although prophylaxis can be considered therapy), this being sufficient to show benefit to the individual. The actual amount administered, and rate and time-course of administration, will depend on the nature and severity of protein aggregation disease being treated. Prescription of treatment, e.g. decisions on dosage etc., is within the responsibility of general practitioners and other medical doctors, and typically takes account of the disorder to be treated, the condition of the individual subject, the site of delivery, the method of administration and other factors known to practitioners. Examples of the techniques and protocols mentioned above can be found in Remington's Pharmaceutical Sciences, 16th edition, Osol, A. (ed), 1980.

EXAMPLES

[00137] Below are examples of specific embodiments for carrying out the methods described in this disclosure. The examples are offered for illustrative purposes only and are not intended to limit the scope of the present invention in any way. Efforts have been made to ensure accuracy with respect to numbers used (e.g., amounts, temperatures, etc.), but some experimental error and deviation should, of course, be allowed for.

[00138] The practice of the present invention will employ, unless otherwise indicated, conventional methods of protein chemistry, biochemistry, recombinant DNA techniques and pharmacology, within the skill of the art. Such techniques are explained fully in the literature. See, e.g., T.E. Creighton, *Proteins: Structures and Molecular Properties* (W.H. Freeman and Company, 1993); A.L. Lehninger, *Biochemistry* (Worth Publishers, Inc., current addition); Sambrook, et al., *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); *Methods In Enzymology* (S. Colowick and N. Kaplan eds., Academic Press, Inc.); *Remington's Pharmaceutical Sciences*, 18th Edition (Easton, Pennsylvania: Mack Publishing Company, 1990); Carey and Sundberg *Advanced Organic Chemistry 3rd Ed.* (Plenum Press) Vols A and B(1992).

Example 1: Treatment of Cancers Harboring Sporadic Mutations in the ATM Serine/Threonine Kinase

Methods

[00139] Both DNA-based and RNA-based molecular profiling was performed. For the DNA analysis, the prevalence of ATM mutations in a canine, pan-cancer dataset using next generation sequencing methods was analyzed.. DNA was isolated for all samples from tissue collected through veterinarians enrolling a patient for genomic and/or transcriptomic analysis. The methodology was left to veterinarian discretion, as most soft tissue biopsies are suitable for analysis. However, all samples in this study were paraffin-embedded tissues submitted as one hematoxylin & eosin stained slide, plus 15-20 unstained sections. Tissue processing and pathology consultation were carried out prior to DNA isolation directly from DNA from paraffin-embedded tissues. Treatment data regarding ATM mutation and subject response to HDAC inhibition is monitored

Results

[00140] Sporadic occurrence of ATM mutation in multiple cancers (7/70 cases, 10%) was found **Tables 1 and 2** and **Figure 12**. ATM mutation was observed in both lymphoid/hematopoietic and solid malignancies. ATM mutations observed included missense, splice site and frameshift variants.

Conclusions

[00141] The prevalence and varied histology of the cancers in which we found ATM mutation mimics findings in human cancer. This is an important observation as ATM defects can be exploited to enhance anticancer therapy. For example, ATM mutant cells, with defective induction of DNA-repair, can be particularly susceptible to DNA damage induced cell death. Some histone deacetylase complex (HDAC) inhibitors potently induce reactive oxygen species and DNA damage. Combining a standard DNA damaging chemotherapeutic with an HDAC inhibitor can provide particularly potent treatment options for ATM mutant tumors.

Example 2: Treatment of canine cancers with Rapamycin

[00142] Canine subjects with cancer were treated with Rapamycin alone or in combination with other anti-cancer agents (**Tables 3 and 12-26**). The subjects were administered Rapamycin orally with a starting dose of 0.1 mg/kg/day and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Rapamycin compared to control subjects.

Example 3: Number and Type of Adverse Effects Reported in Canines treated with Rapamycin.

[00143] Canine subjects with cancer were treated with pharmaceutical compositions comprising Rapamycin and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. Out of 192 canine subjects, 21% of the subjects with clinically reported outcomes experienced adverse effects (**Tables 26 and 27**).

Example 4: Treatment of canine cancers with Dasatinib

[00144] Canine subjects with cancer were treated with Dasatinib alone or in combination with other anti-cancer agents (**Tables 4 and 12-26).** The subjects were administered Dasatinib orally with a starting dose of 0.5-0.7 mg/kg/day and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Dasatinib compared to control subjects.

Example 5: Number and Type of Adverse Effects Reported in Canines treated with Dasatinib.

[00145] Canine subjects with cancer were treated with pharmaceutical compositions comprising Dasatinib and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. Out of 94 canine subjects, 31% of the subjects with clinically reported outcomes experienced adverse effects (**Tables 26 and 27**).

Example 6: Treatment of canine cancers with Lapatinib

[00146] Canine subjects with cancer were treated with Lapatinib alone or in combination with other anti-cancer agents (**Tables 5 and 12-26**). The subjects were administered Lapatinib orally with a starting dose of 5-10 mg/kg/day and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Lapatinib compared to control subjects.

Example 7: Number and Type of Adverse Effects Reported in Canines treated with Lapatinib.

[00147] Canine subjects with cancer were treated with pharmaceutical compositions comprising Lapatinib and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. Out of 162 canine subjects, 22% of the subjects with clinically reported outcomes experienced adverse effects (**Tables 26 and 27**).

Example 8: Treatment of canine cancers with Trametinib

[00148] Canine subjects with cancer were treated with Trametinib alone or in combination with other anti-cancer agents (**Tables 6 and 12-26**). The subjects were administered Trametinib orally with a starting dose of 0.02 mg/kg/day and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Trametinib compared to control subjects.

Example 9: Number and Type of Adverse Effects Reported in Canines treated with Trametinib.

[00149] Canine subjects with cancer were treated with pharmaceutical compositions comprising Trametinib and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. Out of 275 canine subjects, 24% of the subjects with clinically reported outcomes experienced adverse effects (**Tables 26 and 27**).

Example 10: Treatment of canine cancers with Vorinostat

[00150] Canine subjects with cancer were treated with Vorinostat alone or in combination with other anti-cancer agents (**Tables 7 and 12-26**). The subjects were administered Vorinostat orally with a starting dose of 30-60 mg/kg/every other day and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Vorinostat compared to control subjects.

Example 11: Number and Type of Adverse Effects Reported in Canines treated with Vorinostat.

[00151] Canine subjects with cancer were treated with pharmaceutical compositions comprising Vorinostat and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. Out of 89 canine subjects, 34% of the subjects with clinically reported outcomes experienced adverse effects (**Tables 27 and 28**).

Example 12: Treatment of canine cancers with Imatinib

[00152] Canine subjects with cancer were treated with Imatinib alone or in combination with other anti-cancer agents (**Table 8**). The subjects were administered Imatinib orally with a starting dose of 10 mg/kg/day and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Imatinib compared to control subjects.

Example 13: Number and Type of Adverse Effects Reported in Canines treated with Imatinib.

[00153] Canine subjects with cancer were treated with pharmaceutical compositions comprising Imatinib and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. Out of 83 canine subjects, 24% of the subjects with clinically reported outcomes experienced adverse effects (**Tables 27 and 28**).

Example 14: Treatment of canine cancers with Crizotinib

[00154] Canine subjects with cancer were treated with Crizotinib alone or in combination with other anti-cancer agents (**Table 9 and 12-26**). The subjects were administered Crizotinib orally with a starting dose of 1 mg/kg/day-2 mg/kg/day and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Crizotinib compared to control subjects.

Example 15: Number and Type of Adverse Effects Reported in Canines treated with Crizotinib.

[00155] Canine subjects with cancer were treated with pharmaceutical compositions comprising Crizotinib and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. Out of 9 canine subjects, 43% of the subjects with clinically reported outcomes experienced adverse effects (**Tables 27 and 28**).

Example 16: Treatment of canine cancers with Sorafenib

[00156] Canine subjects with cancer were treated with Sorafenib alone or in combination with other anti-cancer agents (**Tables 10 and 12-26**). The subjects were administered Sorafenib orally with a starting dose of 1 mg/kg/day-3 mg/kg/day or 1 mg/kg/day-3 mg/kg/week and were monitored for disease progression compared to historical controls. There is a significant improvement in overall survival in subjects treated with Sorafenib compared to control subjects.

Example 17: Number and Type of Adverse Effects Reported in Canines treated with Sorafenib.

[00157] Canine subjects with cancer were treated with pharmaceutical compositions comprising Sorafenib and were monitored for adverse effects including: diarrhea, vomiting inappetence, lethargy, skin lesions, progressive liver enzyme evaluations, increased cardiac toxicity and hemorrhagic gastroenteritis. A minority of subjects with clinically reported outcomes experience adverse effects.

Example 18: Increased Median Survival of Canine Subjects with Cancers After Treatment with Targeted Therapies

[00158] The median survival of subjects treated with targeted therapies comprising, HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof versus subjects treated with traditional non-targeted therapies was determined (**Figure 1**). There was an increase in median survival in subjects with transitional cell carcinoma, thyroid cancer, squamous cell carcinoma, soft tissue sarcoma, pulmonary adenocarcinoma, osteosarcoma, melanoma, mast cell tumor, histiocytic sarcoma, hepatocellular carcinoma and AGASACA.

Example 19: Increased Survival of Canine Subjects with Splenic Hemangiosarcoma Treated with Targeted Therapies

[00159] Survival of subjects with splenic hemangiosarcoma that have been either treated with chemotherapy and splenectomy alone ("control") or treated with targeted therapy and chemotherapy and splenectomy ("treated") was determined (**Figure 2**). There was a significant increase in the probability of survival in subjects treated with targeted therapies versus patients with splenectomy and traditional chemotherapy alone.

Example 20: Increased Survival of Canine Subjects with Transitional Cell Carcinoma and/or Urinary Cancer Harboring BRAF Mutations

Canine subjects with Transitional Cell Carcinoma (TCC) and/or Urinary Cancer (UC) harboring a BRAF mutation were treated with targeted drugs (Trametinib, Lapatinib or Lapatinib and Trametinib) with or without standard chemotherapy and a COX2 inhibitor (**Figure 3**). Trametinib was administered at a dose of 0.02-0.03 mg/kg orally, daily.

Lapatinib was administered at a dose of 5-10 mg/kg orally once daily. Subjects treated with the targeted drugs exceeded published median survival times (MST) for either Cox inhibitor treatment alone (195 days) or chemotherapy and Cox2 inhibitor treatment (291 days).

[00160] While the invention has been particularly shown and described with reference to a preferred embodiment and various alternate embodiments, it will be understood by persons skilled in the relevant art that various changes in form and details can be made therein without departing from the spirit and scope of the invention.

[00161] All references, issued patents and patent applications cited within the body of the instant specification are hereby incorporated by reference in their entirety, for all purposes.

TABLES

Table 1Cancer Type	Group	Cohort Size (# Dogs)	Median Survival Time (Days)	Common Drugs*	Most Common Biomarker(s)
Transitional Cell Carcinoma	Overall	50	205		BRAF
Transitional Cell Carcinoma	Targeted Therapy	40	257.5	Lapatinib Trametinib	
Transitional Cell Carcinoma	Traditional Therapy Only	10	78		
Thyroid Cancer	Overall	4	621.5		NOTCH1
Thyroid Cancer	Targeted Therapy	3	1007	Trametinib Lapatinib Rapamycin	
Thyroid Cancer	Traditional Therapy Only	1	34		
T Cell Lymphoma	Overall	6	126		
T Cell Lymphoma	Targeted Therapy	3	126		
T Cell Lymphoma	Traditional Therapy Only	2	186.5		
Squamous Cell Carcinoma	Overall	12	193		PDGFRβ SETD2
Squamous Cell Carcinoma	Targeted Therapy	11	237	Trametinib Lapatinib	
Squamous Cell Carcinoma	Traditional Therapy Only	1	75		
Soft Tissue Sarcoma	Overall	14	327		
Soft Tissue Sarcoma	Targeted Therapy	11	370	Trametinib Dasatinib Rapamycin	SETD2 ATM
Soft Tissue Sarcoma	Traditional Therapy Only	3	40		
Pulmonary Adenocarcinoma	Overall	7	118		

Table 1Cancer Type	Group	Cohort Size (# Dogs)	Median Survival Time (Days)	Common Drugs*	Most Common Biomarker(s)
Pulmonary Adenocarcinoma	Targeted Therapy	5	118	Lapatinib Trametinib	
Pulmonary Adenocarcinoma	Traditional Therapy Only	2	100.5		
Osteosarcoma	Overall	24	153.5		SETD2
Osteosarcoma	Targeted Therapy	18	1555.5	Dasatinib Rapamycin	
Osteosarcoma	Traditional Therapy Only	6	49.5		
Melanoma	Overall	26	231.5		SETD2
Melanoma	Targeted Therapy	21	239	Trametinib Dasatinib Rapamycin	
Melanoma	Traditional Therapy Only	5	111		
Mast Cell Tumor	Overall	31	254		SETD2 PDGFRβ NOTCH1
Mast Cell Tumor	Targeted Therapy	19	289	Imatinib	
Mast Cell Tumor	Traditional Therapy Only	12	234.5		
Mammary Carcinoma	Overall	6	135		
Mammary Carcinoma	Targeted Therapy	4	135		
Mammary Carcinoma	Traditional Therapy Only	2	217		
Lymphoma	Overall	25	194		
Lymphoma	Targeted Therapy	16	188		
Lymphoma	Traditional Therapy Only	9	250		
Histiocytic Sarcoma	Overall	21	138.5		

Table 1Cancer Type	Group	Cohort Size (# Dogs)	Median Survival Time (Days)	Common Drugs*	Most Common Biomarker(s)
Histiocytic Sarcoma	Targeted Therapy	15	162	Vorinostat Trametinib	
Histiocytic Sarcoma	Traditional Therapy Only	7	50		
Hepatocellular Carcinoma	Overall	7	285		
Hepatocellular Carcinoma	Targeted Therapy	5	285	Vorinostat Rapamycin	
Hepatocellular Carcinoma	Traditional Therapy Only	2	207		
Hemangiosarcoma	Overall	81	119		IK3CA; p53; PTEN; NOTCH1
Hemangiosarcoma	Targeted Therapy	54	133	Rapamycin Trametinib Daasatinib Vorinostat	
Hemangiosarcoma	Traditional Therapy Only	27	45		
Apocrine gland anal sac adenocarcinomas (AGASACA)	Overall	12	523.5		
	Targeted Therapy	10	560.5	Lapatinib Trametinib	
	Traditional Therapy Only	2	351.5		

*For each drug the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Lapatinib 5-10 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Sorafenib - 3 mg/kg/day orally once daily or 3 mg/kg orally once weekly)

Table 2:

Case Details					ATM Mutations						
Case #	**Sex**	**Breed**	**Histology**	**Location**	**Position on Chr. 5**	**Gene**	**Wildtype DNA**	**DNA Change**	**Type of Mutation**	**Nucleotide Change**	**Amino Acid Change**
1	Male	Golden Retriever	Histiocytic sarcoma	Spleen	24214063	ATM	G	A	Splice Variant	6109C>T	
2	Female	German Shepherd	B-Cell Lymphoma	Distal ileum, omentum, left kidney	24261328	ATM	TAC	T	Frameshift	2722_2723delGT	Val908fe
3	Male	Boxer	T-cell Lymphoma	Multi centric	24203777	ATM	G	T	Missense	7589C>A	Thr2530Asn
4	Male	Yorkshire Terrier	B-cell lymphoma	Multi centric	24261328	ATM	TAC	T	Frameshift	2722_2723delGT	Val908fe
5	Female	Boxer	Osteosarcoma	Proximal tibia, pulmonary metastatic disease	24251038	ATM	T	A	Missense	3431 A>T	His1144Leu
6	Female	Labrador Retriever	Hemangiosarcoma	Spleen, metastatic disease	24258517	ATM	G	A	Missense	2966OT	Ala989Val
7	Female	Greyhound	Soft tissue sarcoma	Left Elbow, high grade	24226831 24251038	ATM ATM	A T	G A	Missense Missense	5267T>C. 3431 A>T	Met1756Thr His1144Leu
8	Male	Yorkshire Terrier	Soft tissue sarcoma	Left shoulder, grade II	24265200	ATM	T	G	Missense	2132A>C	Asp711Ala
9	Male	Australian Cattle Dog	Melanoma (Oral)	Dorsal/Caudal Tongue	24243009	ATM	G	C	Missense	4083OG	Ser1361Arg
10	Male	yorkie	Adenocarcinoma	sino nasal / pharynx	24265200	ATM	T	G	Missense	2132A>C	Asp711Ala
11	Female	Staffordshire Terrier	Transitional Cell Carcinoma	urinary bladder	24228027	ATM	C	G	Missense	5173G>C	Glu1725Gln
12	Female	Labrador Retriever	Hemangiosarcoma	Subcutaneous, grade II	24258517	ATM	G	A	Missense	2966C>T	Ala989Val
13	Male	Labrador Mix	Spindle Cell Sarcoma	Distal Radius	24258517	ATM	G	A	Missense	2966C>T	Ala989Val
14	Female	Labrador Retriever	Anaplastic carcinoma	ventral left cervical mass	24258517	ATM	G	A	Missense	2966C>T	Ala989Val
15	Male	Australian Cattle dog	Squamous cell carcinoma	Right tonsil, right medial	24193080	ATM	CT	C	Missense	8445delA	Glu2815fs

				retropharyngeal lymph node							

Table 3: Treatment Details

Case#	Piror Treatment	Treatments	Status (as of 10/04/19)	Time on Treatment (days)	Notes
1	Surgery	Vorinostat (ended 10/1/18)	Alive	188	Vorinostat given for 6 months after surgery
2	CHOP, surgery, elspar, cytoxan, CCNU, activated T cells	Trametinib, Vorinostat, Apoquel, Rapamycin	Alive	80	Targeted drugs given only with recurrence
3	CHOP	Trametinib, Vorinostat, Apoquel	Deceased	66	Targeted drugs given only with recurrence
4	CHOP		Alive		Remission; wailing for recurrence to start targeted therapy
5	Carboplatin, T-Cell therapy		Deceased		Treatment following FidoCure diagnostic unknown
6	None.	Imatinib, Rapamycin	Alive	121	Prescription tilled 6x
7	Carboplatin, cytoxan, Chlorambucil	Dasatinib, Rapamycin	Alive	79	Targeted treatment started following tumor recurrence
8	None	Trametinib, Rapamycin, Imatinib	Alive	92	Switched to Imatinib 9/12/19 with progression
9	Canine Melanoma Vaccine	Dasatinib, Rapamycin	Deceased	48	Targeted drugs given when progressive disease
10	Palladia	Rapamycin, Dasatinib	Alive	34	Also has heart disease, hypertension, collapsing trachea and CLL (stable)
11	Radiation, Mitoxantrone	Lapatinib, Trametinib	Alive	58	Currently on Trametinib only
12	None	Trametinib	Alive	17	
13	Unknown	Trametinib	Alive	18	
14	Surgery, Palladia	Dasatinib, Rapamycin	Alive	13	Targeted drugs given when progressive disease
15	Unknown		Alive		New case

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Table 4

Case #	Tumor type	Tumor Grade	Tumor Location	Drug Treatment*
1	Adenocarcinoma		sino nasal / pharynx	Rapamycin, Dasatinib
2	Anal - Apocrine gland anal sac adenocarcinoma	low grade	L anal sac	Dasatinib, Rapamycin
3	Anal - Apocrine gland anal sac adenocarcinoma		right anal gland	Piroxicam, Toceranib, Lapatinib, Rapamycin, Trametinib
4	Anal - Apocrine gland anal sac adenocarcinoma	Intermediate grade	R anal gland; previous anal sac removed from L anal gland 2.5 years ago	Rapamycin, Trametinib
5	B-cell lymphoma	unknown	Peripheral lymph node	Rapamycin, Trametinib, Lomustine
6	Hemangiosarcoma		Spleen	Imatinib, Rapamycin
7	Hemangiosarcoma	Spleen		Imatinib, Rapamycin
8	Hemangiosarcoma		Primary tumor in the spleen with metastasis to the liver	Rapamycin
9	Hemangiosarcoma	High	Spleen	Rapamycin
10	Hemangiosarcoma	Unknown - ?	Free floating - caudal abdominal. Right hepatic liver mass.	Rapamycin, Imatinib
11	Hemangiosarcoma	1	Spleen	Rapamycin, Imatinib
12	Hemangiosarcoma	3	Spleen	Rapamycin, Imatinib
13	Hemangiosarcoma		Spleen	Rapamycin, Vorinostat
14	Hemangiosarcoma		Spleen	Trametinib, Rapamycin
15	Hemangiosarcoma		spleen	Trametinib, Rapamycin
16	Hemangiosarcoma	Intermediate	Liver, subcutaneous and lung nodules	Trametinib, Toceranib, Rapamycin, Imatinib

17	Hemangiosarcoma	-	Spleen	Vorinostat, Dasatinib, Rapamycin
18	Hemangiosarcoma	unknown	spleen	Vorinostat, Rapamycin, Imatinib
19	Hemangiosarcoma		Spleen	Trametinib, Rapamycin
20	Hemangiosarcoma - Presumptive, Right Atrial	Unknown	Right Atrium	Rapamycin, Imatinib, Apoquel
21	Hemangiosarcoma - splenic, liver nodules			Trametinib, Rapamycin
22	Hemangiosarcoma (Perirenal)		right kidney	Rapamycin, Imatinib, Apoquel
23	Hemangiosarcoma (Retroperitoneal)		Right body wall	Rapamycin, Imatinib
24	Hemangiosarcoma (spleen)		Spleen, Liver	Trametinib, Rapamycin
25	Hemangiosarcoma (Suspected)		Liver	Imatinib, Rapamycin
26	Hepatocellular carcinoma	Well differentiated (MI = 18)	Multiple liver lobectomies - with now presumed multiple target lesions on abdominal ultrasound and cytology is consistent with presumed hepatocellular carcinoma.	Rapamycin, Trametinib
27	High grade invasive mammary ductular carcinoma with lymphatic invasion		Right 4th and 5th mammary glands	Imatinib, Rapamycin
28	Histiocytic Sarcoma	high grade	right rear leg, caudal distal femur	Rapamycin, Trametinib
29	Histiocytic sarcoma		R cranial lung lobe	Dasatinib, Rapamycin
30	Histiocytic sarcoma	poorly differentiated	liver and omentum	Rapamycin, Vorinostat, Erlotinib, Trametinib

31	Histiocytic sarcoma		lobulated spleen with ill-defined hypoechoic nodules & coarse echotexture	Trametinib, Rapamycin
32	Histiocytic sarcoma		Left shoulder	Vorinostat, Rapamycin
33	Histiocytic sarcoma		left axilla	Rapamycin, Apoquel, Trametinib
34	Histiocytic sarcoma		L stifle, L medial iliac and visceral lymph nodes	Rapamycin, Dasatinib
35	Histiocytic sarcoma - Pulmonary		Right cranial lung lobe	Rapamycin
36	Leiomyosarcoma	low grade	vagina	Imatinib, Rapamycin
37	Leiomyosarcoma		Liver	Trametinib, Rapamycin
38	Lymphoma			Rapamycin, Dasatinib
39	Lymphoma		CNS, GI, Ocular	Trametinib, Rapamycin, Cytarabine
40	Mammary carcinoma	unknown	mammary glands L3-5	Trametinib, Rapamycin
41	Mammary Gland Carcinoma	High Grade (Grade 3)	Right mammary chain, first gland	Rapamycin, Dasatinib
42	Mammary tumor	0	mammary tissue	Rapamycin, Trametinib
43	Mast cell tumor	High Grade	Right Flank	Imatinib, Sorafenib, Rapamycin
44	Melanoma	Mitotic Index Count 16	Lower left Jaw	Rapamycin, Dasatinib
45	Melanoma		Oral submucosa	Dasatinib, Deramaxx, Rapamycin, Palladia

46	Melanoma	MI 15	R Forelimb Prescapular Area		Rapamycin, Trametinib
47	Melanoma	Malignant 6 mitosis in 10hpfs	Fourth Digit Right Forepaw, lungs, right shoulder		Rapamycin, Trametinib
48	Melanoma	none	left submandibular lymph node (metastasis from oral melanoma originally removed from lip)		Rapamycin, Trametinib
49	Melanoma		Tongue base		Trametinib, Rapamycin
50	Melanoma (Oral)		Dorsal/Caudal Tongue		Dasatinib, Rapamycin
51	Melanoma (Oral)		Lip and lymph node		Rapamycin, Dasatinib
52	Melanoma (Oral)		right upper lip		Rapamycin, Dasatinib, Trametinib
53	Metastatic Apocrine gland anal sac adenocarcinoma	High grade, 3-7 mitotic figures per high power field	Left Inguinal Lymphnode, Perivulvar, Now dorsal and left of bladder trigone and urethra area		Rapamycin, Lapatinib
54	Myxosarcoma	Grade 1	R abdominal wall		Rapamycin, Imatinib
55	Nasal adenocarcinoma		Left choana		Trametinib, Rapamycin
56	Osteosarcoma		L proximal humerus		Dasatinib, Rapamycin
57	Osteosarcoma		maxilla, right		Dasatinib, Rapamycin

58	Osteosarcoma	Right distal tibia		Rapamycin, Dasatinib, Trametinib
59	Osteosarcoma	unknown	proximal humerus	Vorinostat, Rapamycin, Meloxicam, Sorafenib, Dasatinib, Crizotinib, Erlotinib
60	Osteosarcoma	UNKNOWN	LEFT MAXILLARY	Trametinib, Dasatinib, Rapamycin
61	Pancreatic carcinoma	NA	pancreas, intra-abdominal lymph nodes	Piroxicam, Trametinib, Rapamycin
62	Peripheral nerve sheath tumor	Grade 1	left muzzle skin	Dasatinib, Rapamycin
63	Right Atrial Presumptive Hemangiosarcoma	Highly metastatic biological behavior	Right Atrial	Imatinib, Rapamycin
64	Sarcoma	no grading scheme	Rectum	Trametinib, Rapamycin
65	Sarcoma		left nasal cavity with intracranial extension	Dasatinib, Rapamycin, Trametinib, Vorinostat
66	Sarcoma		Left medial/caudal pelvic limb, metastases to thorax	Rapamycin, Trametinib, Imatinib, Vorinostat
67	Sarcoma, likely metastatic osteosarcoma	High	R Middle Lung Lobe; R Caudal Lung Lobe	Rapamycin, Dasatinib
68	Soft tissue sarcoma	High grade; incompletely Excised	Left Elbow	Dasatinib, Rapamycin
69	Soft tissue sarcoma	low	Ventral thorax	Rapamycin, Dasatinib, Trametinib
70	Soft tissue sarcoma	Low-intermediate	Right lateral thorax	Rapamycin, Imatinib
71	Soft tissue sarcoma		Left Axillary	Trametinib, Rapamycin
72	Soft tissue sarcoma	grade II	left shoulder	Trametinib, Rapamycin
73	Soft tissue sarcoma	2	right shoulder	Vorinostat, Rapamycin, Dasatinib
74	Spindle cell sarcoma	Grade III	spleen	Rapamycin, Trametinib

75	Squamous Cell Carcinoma	High	Primary site unknown; pulmonary metastasis, SQ	Rapamycin, Trametinib
76	Squamous cell carcinoma		Tonsillar region, retropharyngeal lymph node	Trametinib, Toceranib, Rapamycin
77	Stromal Sarcoma (spleen)	Low based on splenic tumor histopathology	Spleen, liver	Imatinib, Rapamycin, Trametinib
78	Stromal sarcoma (spleen)	na	spleen	Rapamycin, Dasatinib
79	Subcutaneous Hemangiosarcoma		regrowth left flank and regional lymph node	Rapamycin, Dasatinib
80	Thyroid carcinoma - Metastatic	Completely Excised	Cervical Mass	Rapamycin, Imatinib
81	Presumptive Hemangiosarcoma	n/a	n/a	Imatinib, Rapamycin

*For each drug the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Lapatinib 5-10 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Sorafenib - 3 mg/kg/day orally once daily or 3 mg/kg orally once weekly)

Table 5

Case #	Tumor type	Tumor Grade	Tumor Location	Drug Treatment*
1	Adenocarcinoma		sino nasal / pharynx	Dasatinib, Dasatinib
2	Anal - Apocrine gland anal sac adenocarcinoma	low grade	L anal sac	Dasatinib, Dasatinib
3	Anal - Apocrine gland anal sac adenocarcinoma		right anal gland	Piroxicam, Toceranib, Lapatinib, Dasatinib, Trametinib

4	Anal - Apocrine gland anal sac adenocarcinoma	Intermediate grade	R anal gland; previous anal sac removed from L anal gland 2.5 years ago	Dasatinib, Trametinib
5	B-cell lymphoma	unknown	Peripheral lymph node	Dasatinib, Trametinib, Lomustine
6	Hemangiosarcoma		Spleen	Imatinib, Dasatinib
7	Hemangiosarcoma	Spleen		Imatinib, Dasatinib
8	Hemangiosarcoma		Primary tumor in the spleen with metastasis to the liver	Dasatinib
9	Hemangiosarcoma	High	Spleen	Dasatinib
10	Hemangiosarcoma	Unknown - ?	Free floating - caudal abdominal. Right hepatic liver mass.	Dasatinib, Imatinib
11	Hemangiosarcoma	1	Spleen	Dasatinib, Imatinib
12	Hemangiosarcoma	3	Spleen	Dasatinib, Imatinib
13	Hemangiosarcoma		Spleen	Dasatinib, Vorinostat
14	Hemangiosarcoma		Spleen	Trametinib, Dasatinib
15	Hemangiosarcoma		spleen	Trametinib, Dasatinib
16	Hemangiosarcoma	Intermediate	Liver, subcutaneous and lung nodules	Trametinib, Toceranib, Dasatinib, Imatinib
17	Hemangiosarcoma	-	Spleen	Vorinostat, Dasatinib, Dasatinib
18	Hemangiosarcoma	unknown	spleen	Vorinostat, Dasatinib, Imatinib
19	Hemangiosarcoma		Spleen	Trametinib, Dasatinib
20	Hemangiosarcoma - Presumptive, Right Atrial	Unknown	Right Atrium	Dasatinib, Imatinib, Apoquel
21	Hemangiosarcoma - splenic, liver nodules			Trametinib, Dasatinib

22	Hemangiosarcoma (Perirenal)		right kidney	Dasatinib, Imatinib, Apoquel
23	Hemangiosarcoma (Retroperitoneal)		Right body wall	Dasatinib, Imatinib
24	Hemangiosarcoma (spleen)		Spleen, Liver	Trametinib, Dasatinib
25	Hemangiosarcoma (Suspected)		Liver	Imatinib, Dasatinib
26	Hepatocellular carcinoma	Well differentiated (MI = 18)	Multiple liver lobectomies - with now presumed multiple target lesions on abdominal ultrasound and cytology is consistent with presumed hepatocellular carcinoma.	Dasatinib, Trametinib
27	High grade invasive mammary ductular carcinoma with lymphatic invasion		Right 4th and 5th mammary glands	Imatinib, Dasatinib
28	Histiocytic Sarcoma	high grade	right rear leg, caudal distal femur	Dasatinib, Trametinib
29	Histiocytic sarcoma		R cranial lung lobe	Dasatinib, Dasatinib
30	Histiocytic sarcoma	poorly differentiated	liver and omentum	Dasatinib, Vorinostat, Erlotinib, Trametinib
31	Histiocytic sarcoma		lobulated spleen with ill-defined hypoechoic nodules & coarse echotexture	Trametinib, Dasatinib
32	Histiocytic sarcoma		Left shoulder	Vorinostat, Dasatinib
33	Histiocytic sarcoma		left axilla	Dasatinib, Apoquel, Trametinib
34	Histiocytic sarcoma		L stifle, L medial iliac and visceral lymph nodes	Dasatinib, Dasatinib
35	Histiocytic sarcoma - Pulmonary		Right cranial lung lobe	Dasatinib
36	Leiomyosarcoma	low grade	vagina	Imatinib, Dasatinib
37	Leiomyosarcoma		Liver	Trametinib, Dasatinib

38	Lymphoma			Dasatinib, Dasatinib
39	Lymphoma		CNS, GI, Ocular	Trametinib, Dasatinib, Cytarabine
40	Mammary carcinoma	unknown	mammary glands L3-5	Trametinib, Dasatinib
41	Mammary Gland Carcinoma	High Grade (Grade 3)	Right mammary chain, first gland	Dasatinib, Dasatinib
42	Mammary tumor	0	mammary tissue	Dasatinib, Trametinib
43	Mast cell tumor	High Grade	Right Flank	Imatinib, Sorafenib, Dasatinib
44	Melanoma	MItotic Count 16	Lower left Jaw	Dasatinib, Dasatinib
45	Melanoma		Oral submucosa	Dasatinib, Deramaxx, Dasatinib, Palladia
46	Melanoma	MI 15	R Forelimb Prescapular Area	Dasatinib, Trametinib
47	Melanoma	Malignant 6 mitosis in 10hpfs	Fourth Digit Right Forepaw, lungs, right shoulder	Dasatinib, Trametinib
48	Melanoma	none	left submandibular lymph node (metastasis from oral melanoma originally removed from lip)	Dasatinib, Trametinib
49	Melanoma		Tongue base	Trametinib, Dasatinib
50	Melanoma (Oral)		Dorsal/Caudal Tongue	Dasatinib, Dasatinib
51	Melanoma (Oral)		Lip and lymph node	Dasatinib, Dasatinib
52	Melanoma (Oral)		right upper lip	Dasatinib, Dasatinib, Trametinib
53	Metastatic Apocrine gland anal sac adenocarcinoma	High grade, 3-7 mitotic figures per high power field	Left Inguinal Lymphnode, Perivulvar, Now dorsal and left of bladder trigone and urethra area	Dasatinib, Lapatinib

54	Myxosarcoma	Grade 1	R abdominal wall	Dasatinib, Imatinib
55	Nasal adenocarcinoma		Left choana	Trametinib, Dasatinib
56	Osteosarcoma		L proximal humerus	Dasatinib, Dasatinib
57	Osteosarcoma		maxilla, right	Dasatinib, Dasatinib
58	Osteosarcoma	Right distal tibia		Dasatinib, Dasatinib, Trametinib
59	Osteosarcoma	unknown	proximal humerus	Vorinostat, Dasatinib, Meloxicam, Sorafenib, Dasatinib, Crizotinib, Erlotinib
60	Osteosarcoma	Unknown	Left Maxillary	Trametinib, Dasatinib, Dasatinib
61	Pancreatic carcinoma	NA	pancreas, intra-abdominal lymph nodes	Piroxicam, Trametinib, Dasatinib
62	Peripheral nerve sheath tumor	Grade 1	left muzzle skin	Dasatinib, Dasatinib
63	Right Atrial Presumptive Hemangiosarcoma	Highly metastatic biological behavior	Right Atrial	Imatinib, Dasatinib
64	Sarcoma	no grading scheme	Rectum	Trametinib, Dasatinib
65	Sarcoma		left nasal cavity with intracranial extension	Dasatinib, Dasatinib, Trametinib, Vorinostat
66	Sarcoma		Left medial/caudal pelvic limb, metastasess to thorax	Dasatinib, Trametinib, Imatinib, Vorinostat
67	Sarcoma, likely metastatic osteosarcoma	High	R Middle Lung Lobe; R Caudal Lung Lobe	Dasatinib, Dasatinib
68	Soft tissue sarcoma	High grade; incompletely Excised	Left Elbow	Dasatinib, Dasatinib
69	Soft tissue sarcoma	low	Ventral thorax	Dasatinib, Dasatinib, Trametinib
70	Soft tissue sarcoma	Low-intermediate	Right lateral thorax	Dasatinib, Imatinib
71	Soft tissue sarcoma		Left Axillary	Trametinib, Dasatinib

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72	Soft tissue sarcoma	grade II	left shoulder	Trametinib, Dasatinib
73	Soft tissue sarcoma	2	right shoulder	Vorinostat, Dasatinib, Dasatinib
74	Spindle cell sarcoma	Grade III	spleen	Dasatinib, Trametinib
75	Squamous Cell Carcinoma	High	Primary site unknown; pulmonary metastasis, SQ	Dasatinib, Trametinib
76	Squamous cell carcinoma		Tonsillar region, retropharyngeal lymph node	Trametinib, Toceranib, Dasatinib
77	Stromal Sarcoma (spleen)	Low based on splenic tumor histopathology	Spleen, liver	Imatinib, Dasatinib, Trametinib
78	Stromal sarcoma (spleen)	na	spleen	Dasatinib, Dasatinib
79	Subcutaneous Hemangiosarcoma		regrowth left flank and regional lymph node	Dasatinib, Dasatinib
80	Thyroid carcinoma - Metastatic	Completely Excised	Cervical Mass	Dasatinib, Imatinib
81	Presumptive Hemangiosarcoma	n/a	n/a	Imatinib, Dasatinib

*For each drug the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Lapatinib 5-10 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Sorafenib - 3 mg/kg/day orally once daily or 3 mg/kg orally once weekly)

Table 6

Case #	Tumor type	Tumor Grade	Tumor Location	Drug Treatment*

1	Hepatoma - Benign		liver	Lapatinib
2	Anal - Apocrine gland adenocarcinoma	Mitotic index is 3 mitotic figures in 10 high powered fields. Metastases is common & already present indicating poor prognosis.	Anal Sac Gland	Lapatinib
3	Anal - Apocrine gland anal sac adenocarcinoma	N/A	Right anal gland	Lapatinib
4	Anal - Apocrine gland anal sac adenocarcinoma		Rright anal gland	Piroxicam, Toceranib, Lapatinib, Rapamycin, Trametinib
5	Anal - Apocrine gland anal sac adenocarcinoma (AGASACA)	MI=9	Left anal gland mass	Lapatinib
6	Anal - Metastatic apocrine gland adenocarcinoma	High grade, 3-7 mitotic figures per high power field	Left Inguinal Lymph node, Perivulvar, Now dorsal and left of bladder trigone and urethra area	Rapamycin, Lapatinib
7	Anal Sac Adenocarcinoma		Pulmonary Metastasis	Lapatinib
8	Anal Sac Adenocarinoma		Pulmonary metastatic disease	Lapatinib
9	Carcinoma - metastatic, primary site unspecified	n/a	Pericardium, lungs	Lapatinib
10	Fibrosarcoma	High/Low	Lmaxilla/zygomatic arch	Lapatinib
11	Insulinoma	0	lymph node and pancreas	Lapatinib, Toceranib
12	Mammary carcinoma - mixed type, grade II	grade II	left m4	Lapatinib
13	Myoepithelioma – Malignant		4th right mammary gland	Lapatinib
14	Plasma cell tumor			Lapatinib
15	Prostatic	N/A	Prostate	Lapatinib
16	Pulmonary - primary and metastatic neoplasia	unknown	all lung fields	Lapatinib, Trametinib
17	Pulmonary - unspecified			Lapatinib

18	Pulmonary adenocarcinoma		cranial medastinal mass	Lapatinib, Trametinib
19	Pulmonary carcinoma	n/a	Diffuse through lungs	Lapatinib
20	Sarcoma (neurofibrosarcoma)	na	body wall	Lapatinib
21	Squamous cell carcinoma		Left Tonsil	Lapatinib
22	Transitional Cell Carcinoma	unknown	Apical mural margin mass into the urinary bladder lumen	Lapatinib
23	Transitional Cell Carcinoma	unknown	Bladder / trigonal area	Lapatinib
24	Transitional Cell Carcinoma		Trigone	Lapatinib
25	Transitional Cell Carcinoma		Bladder/urethra	Lapatinib
26	Transitional Cell Carcinoma		urinary bladder	Lapatinib
27	Transitional Cell Carcinoma	none	Bladder	Lapatinib
28	Transitional Cell Carcinoma		Bladder	Lapatinib
29	Transitional Cell Carcinoma	n/a	bladder	Lapatinib
30	Transitional Cell Carcinoma		Bladder	Lapatinib, Carprofen, Trametinib
31	Transitional Cell Carcinoma	unknown	bladder	Lapatinib, Trametinib
32	Transitional Cell Carcinoma	0	bladder	Lapatinib, Trametinib
33	Transitional Cell Carcinoma		Bladder	Lapatinib, Trametinib
34	Transitional Cell Carcinoma			Lapatinib, Trametinib
35	Transitional Cell Carcinoma		Bladder	Lapatinib, Trametinib
36	Transitional Cell Carcinoma		Bladder and probable urethra	Lapatinib, Trametinib
37	Transitional Cell Carcinoma	not available	Urinary Bladder	Lapatinib, Trametinib
38	Transitional Cell Carcinoma		Urethra	Lapatinib, Trametinib
39	Transitional Cell Carcinoma	0	bladder	Piroxicam, Lapatinib

40	Transitional Cell Carcinoma		Urinary bladder	Trametinib, Lapatinib
41	Transitional Cell Carcinoma		Proximal urethra/urinary bladder, L inguinal lymph node	Trametinib, Lapatinib
42	Transitional Cell Carcinoma		bladder	Trametinib, Lapatinib
43	Transitional Cell Carcinoma Papillary/polypoid minimally invasive variant		Apex of the bladder	Lapatinib
44	Transitional Cell Carcinoma	Pending CADET BRAF Test - - enlarged mesenteric lymph node, an annular mass in colon wall	Bladder, Abdomen, Colon	Trametinib, Lapatinib

*For each drug the following dosages were used:

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Lapatinib 5-10 mg/kg orally once daily

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Table 7

Case #	Tumor type	Tumor Grade	Tumor Location	Drug Treatment*
1	Anal - Apocrine gland anal sac adenocarcinoma		right anal gland	Piroxicam, Toceranib, Lapatinib, Rapamycin, Trametinib
2	Anal - Apocrine gland anal sac adenocarcinoma	Intermediate grade	R anal gland; previous anal sac removed from L anal gland 2.5 years ago	Rapamycin, Trametinib
3	Anal - Apocrine gland anal sac adenocarcinoma		liver, LN	Trametinib
4	B-cell Lymphoma	High grade	Right popliteal lymph node	Trametinib, Vorinostat
5	B-cell lymphoma	unknown	Peripheral lymph node	Rapamycin, Trametinib, Lomustine
6	Gastric carcinoma/gastric mast cell tumor		Stomach (fundus and pylorus)	Crizotinib, Imatinib, Trametinib
7	Gingiva carcinoma - unspecified		jaw	Imatinib, Trametinib, Lapatinib, Rapamycin
8	Hemangiosarcoma		caudal right stifle	Trametinib, Dasatinib
9	Hemangiosarcoma		spleen	Trametinib, Rapamycin
10	Hemangiosarcoma		spleen	Trametinib, Rapamycin
11	Hemangiosarcoma	Intermediate	Liver, subcutaneous and lung nodules	Trametinib, Toceranib, Rapamycin, Imatinib
12	Hemangiosarcoma		Spleen/Liver	Vorinostat, Trametinib
13	Hemangiosarcoma		Spleen	Trametinib, Rapamycin
14	Hemangiosarcoma	0	Left hind leg	Vorinostat, Chlorambucil, Imatinib, Trametinib
15	Hemangiosarcoma - splenic, liver nodules			Trametinib, Rapamycin
16	Hemangiosarcoma (spleen)		Spleen, Liver	Trametinib, Rapamycin
17	Hepatocellular carcinoma	Well differentiated (MI = 18)	Multiple liver lobectomies - with now presumed multiple target lesions on abdominal ultrasound and cytology is consistent with presumed hepatocellular carcinoma.	Rapamycin, Trametinib

18	Histiocytic Sarcoma	high grade	right rear leg, caudal distal femur	Rapamycin, Trametinib
19	Histiocytic Sarcoma		spleen, right middle lung lobe, perirenal LN, SQ dorsal cervical	Trametinib, Rapamycin
20	Histiocytic sarcoma	poorly differentiated	liver and omentum	Rapamycin, Vorinostat, Erlotinib, Trametinib
21	Histiocytic sarcoma		lobulated spleen with ill-defined hypoechoic nodules & coarse echotexture	Trametinib, Rapamycin
22	Histiocytic sarcoma	Grade II	Left Thorax	Vorinostat, Trametinib
23	Histiocytic sarcoma		left axilla	Rapamycin, Apoquel, Trametinib
24	Histiocytic sarcoma	unknown	liver and spleen	Trametinib
25	Histiocytic sarcoma		lungs and node	Trametinib
26	Histiocytic sarcoma	unknown	left stifle	Vorinostat, Crizotinib, Trametinib
27	Leiomyosarcoma		Liver	Trametinib, Rapamycin
28	Lymphoma	intermediate to large cell type	right axilla	Trametinib
29	Lymphoma	high grade	skin	Trametinib
30	Lymphoma		Lymp hnode	Trametinib, Apoquel, Vorinostat
31	Lymphoma		CNS, GI, Ocular	Trametinib, Rapamycin, Cytarabine
32	Lymphoma		Right Oral Mandibular Mass And Right Submandibular Lymph Node	Trametinib, Vorinostat
33	Lymphoma	unknown	distal ileum, omentum, left kidney	Trametinib, Vorinostat, Apoquel
34	Lymphoma - Epitheliotropic		skin	Apoquel, Trametinib
35	Mammary carcinoma	unknown	mammary glands L3-5	Trametinib, Rapamycin
36	Mammary tumor	0	mammary tissue	Rapamycin, Trametinib
37	Mast cell tumor	grade 2/low-grade (MI 1)	left stifle, ventral abdomen	Apoquel, Trametinib
38	Mast cell tumor	Grade 3	Cutaneous	Trametinib
39	Mast cell tumor	unknown	Dorsal thorax	Trametinib, Vorinostat
40	Melanoma	MI 15	R Forelimb Prescapular Area	Rapamycin, Trametinib
41	Melanoma	Malignant 6 mitosis in 10hpfs	Fourth Digit Right Forepaw, lungs, right shoulder	Rapamycin, Trametinib

42	Melanoma	none	left submandibular lymph node (metastasis from oral melanoma originally removed from lip)	Rapamycin, Trametinib
43	Melanoma		Tongue base	Trametinib, Rapamycin
44	Melanoma (Oral)		right upper lip	Rapamycin, Dasatinib, Trametinib
45	Nasal adenocarcinoma		Left choana	Trametinib, Rapamycin
46	Osteosarcoma	Right distal tibia		Rapamycin, Dasatinib, Trametinib
47	Osteosarcoma	UNKNOWN	Left Maxillary	Trametinib, Dasatinib, Rapamycin
48	Pancreatic carcinoma	NA	pancreas, intra-abdominal lymph nodes	Piroxicam, Trametinib, Rapamycin
49	Plasma cell tumor			Lapatinib, Trametinib
50	Pulmonary - Papillary adenocarcinoma	0	Lung	Trametinib
51	Pulmonary - primary and metastatic neoplasia	unknown	all lung fields	Lapatinib, Trametinib
52	Pulmonary adenocarcinoma		cranial medastinal mass	Lapatinib, Trametinib
53	Sarcoma		left nasal cavity with intracranial extension	Dasatinib, Rapamycin, Trametinib, Vorinostat
54	Sarcoma		Left medial/caudal pelvic limb, mets to thorax	Rapamycin, Trametinib, Imatinib, Vorinostat
55	Sarcoma	no grading scheme	Rectum	Trametinib, Rapamycin
56	Soft tissue sarcoma	low	Ventral thorax	Rapamycin, Dasatinib, Trametinib
57	Soft tissue sarcoma		Left Axillary	Trametinib, Rapamycin
58	Soft tissue sarcoma	grade II	left shoulder	Trametinib, Rapamycin, Imatinib
59	Spindle cell sarcoma	Grade III	spleen	Rapamycin, Trametinib
60	Splenic Stromal Sarcoma	High Mitotic Index (27 mitosis in ten 400X fields)	spleen	Trametinib
61	Squamous Cell Carcinoma	High	Primary site unknown; pulmonary metastasis, SQ	Rapamycin, Trametinib
62	Squamous cell carcinoma	unknown	left tonsil	Trametinib
63	Squamous cell carcinoma		Tonsillar region, retropharyngeal lymph node	Trametinib, Toceranib, Rapamycin

64	Stromal Sarcoma (spleen)	Low based on splenic tumor histopathology	Spleen, liver	Imatinib, Rapamycin, Trametinib
65	T-cell Lymphoma	unknown	multicentric	Trametinib, Vorinostat, Apoquel
66	Transitional Cell Carcinoma		Bladder	Lapatinib, Carprofen, Trametinib
67	Transitional Cell Carcinoma	unknown	bladder	Lapatinib, Trametinib
68	Transitional Cell Carcinoma	0	bladder	Lapatinib, Trametinib
69	Transitional Cell Carcinoma		Bladder	Lapatinib, Trametinib
70	Transitional Cell Carcinoma			Lapatinib, Trametinib
71	Transitional Cell Carcinoma		Bladder	Lapatinib, Trametinib
72	Transitional Cell Carcinoma		Bladder and probable urethra	Lapatinib, Trametinib
73	Transitional Cell Carcinoma		Trigone	Lapatinib, Trametinib
74	Transitional Cell Carcinoma	not available	Urinary Bladder	Lapatinib, Trametinib
75	Transitional Cell Carcinoma		Urethra	Lapatinib, Trametinib
76	Transitional Cell Carcinoma	unknown	Apical mural margin mass into the urinary bladder lumen	Lapatinib, Trametinib
77	Transitional Cell Carcinoma		Bladder	Lapatinib, Trametinib
78	Transitional Cell Carcinoma		Bladder	Trametinib
79	Transitional Cell Carcinoma		urethral bladder/trigone	Trametinib
80	Transitional Cell Carcinoma		Bladder	Trametinib
81	Transitional Cell Carcinoma	unknown	URETHRA	Trametinib
82	Transitional Cell Carcinoma	bladder/urethra		Trametinib
83	Transitional Cell Carcinoma		Urinary bladder	Trametinib, Lapatinib
84	Transitional Cell Carcinoma		Proximal urethra/urinary bladder, L inguinal lymph node	Trametinib, Lapatinib
85	Transitional Cell Carcinoma		bladder	Trametinib, Lapatinib
86	Transitional cell carcinoma	Intermediate to high grade	Bladder apex	Trametinib
87	Transitional Cell Carcinoma Papillary/polypoid minimally invasive variant		Apex of the bladder	Lapatinib, Trametinib
88	Transitional cell carcinoma - enlarged mesenteric lymph node, an annular mass in colon wall	Pending CADET BRAF Test	Bladder, Abdomen, Colon	Trametinib, Lapatinib

*For each drug the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Lapatinib 5-10 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Sorafenib - 3 mg/kg/day orally once daily or 3 mg/kg orally once weekly)

Table 8

Case #	Tumor type	Tumor Grade	Tumor Location	Drug Treatment*
1	B-cell Lymphoma		lymph node	Vorinostat
2	B-cell Lymphoma	High grade	Right popliteal lymph node	Trametinib, Vorinostat
3	Hemangiosarcoma		Spleen/Liver	Vorinostat, Trametinib
4	Hemangiosarcoma	unknown	spleen	Vorinostat, Rapamycin, Imatinib
5	Hemangiosarcoma	-	Spleen	Vorinostat, Dasatinib, Rapamycin
6	Hemangiosarcoma		Spleen	Rapamycin, Vorinostat
7	Hemangiosarcoma		spleen	Vorinostat
8	Hemangiosarcoma	0	Left hind leg	Vorinostat, Chlorambucil, Imatinib, Trametinib
9	Histiocytic sarcoma		Left shoulder	Vorinostat, Rapamycin
10	Histiocytic sarcoma	poorly differentiated	liver and omentum	Rapamycin, Vorinostat, Erlotinib, Trametinib
11	Histiocytic sarcoma	Grade II	Left Thorax	Vorinostat, Trametinib
12	Histiocytic sarcoma	unknown	left stifle	Vorinostat, Crizotinib, Trametinib
13	Histiocytic sarcoma		Spleen	Vorinostat
14	Lymphoma	unknown	distal ileum, omentum, left kidney	Trametinib, Vorinostat, Apoquel
15	Lymphoma		Right Oral Mandibular Mass And Right Submandibular Lymph Node	Trametinib, Vorinostat
16	Lymphoma		Lymph node	Trametinib, Apoquel, Vorinostat
17	Lymphoma	High grade	right cervical lymph node	Vorinostat
18	Lymphoma		submandibular lymph node	Vorinostat
19	Mast cell tumor	unknown	Dorsal thorax	Trametinib, Vorinostat
20	Mast cell tumor	3	Lip, Right and left medial elbows, neck	Imatinib, Vorinostat, Chlorambucil, Sorafenib

21	Myxosarcoma	high grade; MI = 20	L medial thigh	Vorinostat, Imatinib
22	Osteosarcoma	unknown	proximal humerus	Vorinostat, Rapamycin, Meloxicam, Sorafenib, Dasatinib, Crizotinib, Erlotinib
23	Sarcoma		Left medial/caudal pelvic limb, metastases to thorax	Rapamycin, Trametinib, Imatinib, Vorinostat
24	Sarcoma		left nasal cavity with intracranial extension	Dasatinib, Rapamycin, Trametinib, Vorinostat
25	Soft tissue sarcoma	2	right shoulder	Vorinostat, Rapamycin, Dasatinib
26	T-cell Lymphoma	unknown	multicentric	Trametinib, Vorinostat, Apoquel

*For each drug, the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Sorafenib - 3 mg/kg/day orally once daily or 3 mg/kg orally once weekly)

Table 9

Case #	Tumor type	Tumor Grade	Tumor Location	Drug Treatment*
1	Gastric carcinoma/gastric mast cell tumor		Stomach (fundus and pylorus)	Crizotinib, Imatinib, Trametinib
2	Gingiva carcinoma - unspecified		jaw	Imatinib, Trametinib, Lapatinib, Rapamycin
3	Hemangiosarcoma	unknown	spleen	Vorinostat, Rapamycin, Imatinib
4	Hemangiosarcoma	Intermediate	Liver, subcutaneous and lung nodules	Trametinib, Toceranib, Rapamycin, Imatinib
5	Hemangiosarcoma		Spleen	Imatinib, Rapamycin
6	Hemangiosarcoma	Unknown - ?	Free floating - caudal abdominal. Right hepatic liver mass.	Rapamycin, Imatinib

7	Hemangiosarcoma	Spleen		Imatinib, Rapamycin
8	Hemangiosarcoma	1	Spleen	Rapamycin, Imatinib
9	Hemangiosarcoma	Spleen	3	Rapamycin, Imatinib
10	Hemangiosarcoma	High	Spleen	Rapamycin, Imatinib
11	Hemangiosarcoma	UNK	Abdominal	Imatinib, Rapamycin
12	Hemangiosarcoma	high	SQ mass L scapular region; diffuse pulmonary metastasis, liver and spleen involvement	Imatinib
13	Hemangiosarcoma	0	Left hind leg	Vorinostat, Chlorambucil, Imatinib, Trametinib
14	Hemangiosarcoma - Presumptive, Right Atrial	Unknown	Right Atrium	Rapamycin, Imatinib, Apoquel
15	Hemangiosarcoma (Perirenal)		right kidney	Rapamycin, Imatinib,Apoquel, Dasatini
16	Hemangiosarcoma (Retroperitoneal)		Right body wall	Rapamcin, Imatinb
17	Hemangiosarcoma (Suspected)		Liver	Imatinib, Rapamycin
18	High grade invasive mammary ductular carcinoma with lymphatic invasion		Right 4th and 5th mammary glands	Imatinib, Rapamycin
19	Histiocytic sarcoma	unknown	left costrochondral junction	Imatinib
20	Leiomyosarcoma	low grade	vagina	Imatinib, Rapamycin
21	Leukemia - ALL or AML			Imatinib
22	Liver and Spleen	Unknown	Liver and Spleen	Imatinib, Rapamycin
23	Mast Cell Tumor			Imatinib
24	Mast cell tumor	unknown	R. Neck	Toceranib, Imatinib
25	Mast cell tumor		Left hip extending to perineum	Imatinib
26	Mast cell tumor	High Grade II	Right side of face, extending into neck	Imatinib

27	Mast cell tumor	3	Lip, Right and left medial elbows, neck	Imatinib, Vorinostat, Chlorambucil, Sorafenib
28	Mast cell tumor		multi focal	Imatinib
29	Mast cell tumor		'-left side of face (1cm) -right medial thigh (0.5cm) -4 preputial and peripreputial (two cranial to prepuce, one right and one left of midline, two on prepuce, one on left and one on right) (range 0.5-1cm) -left ischial region (previous scar) (largest mass, ~1.5cm) -2 perianal masses (one right (1cm), two left (0.5cm)) -left perineal mass (0.5cm) -two masses at right caudomedial thigh (0.5cmeach) 12 total masses removed	Imatinib
30	Mast cell tumor	Grade III	ventral neck	Toceranib, Imatinib
31	Mast cell tumor			Imatinib
32	Mast cell tumor			Imatinib
33	Mast cell tumor	High Grade	Right Flank	Imatinib, Sorafenib, Rapamycin
34	Mast cell tumor		Left Shoulder, Right Flank and tail base	Palladia, Imatinib, Rapamycin
35	Mast cell tumor (Metastatic with early mastocytosis to liver and spleen)		L popliteal lymph node	Imatinib
36	Mast Cell Tumor(s)	Right axilla region	Grade II/high-grade MCT at the right axillary region removed on 12/20/16	Imatinib
37	Myxosarcoma	high grade; MI = 20	L medial thigh	Vorinostat, Imatinib
38	Myxosarcoma	Grade 1	R abdominal wall	Rapamycin, Imatinib
39	Presumptive Hemangiosarcoma	n/a	n/a	Imatinib, Rapamycin
40	Right Atrial Presumptive Hemangiosarcoma	Highly metastatic biological behavior	Right Atrial	Imatinib, Rapamycin

41	Sarcoma		Left medial/caudal pelvic limb, metastases to thorax	Rapamycin, Trametinib, Imatinib, Vorinostat
42	Soft tissue sarcoma	unknown	left caudal hip	Imatinib
43	Soft tissue sarcoma	Low-intermediate	Right lateral thorax	Rapamycin, Imatinib
44	Soft tissue sarcoma	grade II	left shoulder	Trametinib, Rapamycin, Imatinib
45	Stromal Sarcoma (spleen)	Low based on splenic tumor histopathology	Spleen, liver	Imatinib, Rapamycin, Trametinib
46	Thyroid carcinoma - Metastatic	Completely Excised	Cervical Mass	Rapamycin, Imatinib

*For each drug, the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Sorafenib - 3 mg/kg/day orally once daily or 3 mg/kg orally once weekly

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Table 10

Case #	Tumor type	Tumor Grade	Tumor Location	Drug Treatment*
1	Gastric carcinoma/gastric mast cell tumor		Stomach (fundus and pylorus)	Crizotinib, Imatinib, Trametinib
2	Hemangiosarcoma	unknown	Spleen	Toceranib, Crizotinib, Deramaxx
3	Histiocytic sarcoma	unknown	left stifle	Vorinostat, Crizotinib, Trametinib
4	Melanoma	metastatic disease	metastatic lymph node	Toceranib, Crizotinib
5	Osteosarcoma	unknown	proximal humerus	Vorinostat, Rapamycin, Meloxicam, Sorafenib, Dasatinib, Crizotinib, Erlotinib
6	Pulmonary carcinoma with lymphatic invasion		Left Cranial pulmonary Mass	Crizotinib

*For each drug, the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Table 11

Case #	Tumor type	Tumor Grade	Tumor Location	Drugs Treatment*
1	Mast Cell Tumor	Grade III	Left prescap area	Sorafenib
2	Mast cell tumor	3	Lip, Right and left medial elbows, neck	Imatinib, Vorinostat, Chlorambucil, Sorafenib
3	Mast cell tumor	High Grade	Right Flank	Imatinib, Sorafenib, Rapamycin

4	Osteosarcoma	unknown	proximal humerus	Vorinostat, Rapamycin, Meloxicam, Sorafenib, Dasatinib, Crizotinib, Erlotinib

*For each drug, the following dosages were used:

Vorinostat 30 mg/kg orally every other day

Trametinib 0.02-0.03 mg/kg orally once daily

Rapamycin 0.1 mg/kg orally once daily

Lapatinib 5-10 mg/kg orally once daily

Imatinib 10 mg/kg orally once daily

Dasatinib 0.5-0.7 mg/kg orally every other day

Sorafenib 3 mg/kg/day orally once daily or 3 mg/kg orally once weekly

Table 12: Treatment of Transitional Cell Carcinoma

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Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	Prostate		Yes			0		ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2/EGFR inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	prostate, pulmonary nodules on TXR	98	No	Trametinib		0	0	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma		28	**No**	**Lapatinib**	**no**	**0**	**14**	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO AND/OR Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO	
Transitional Cell Carcinoma	Bladder	48	**No**	**Trametinib**	**yes**	**1**	**22**	BRAF: Mutation - V595E (Transitional Cell Carcinoma),ERBB2: Overexpressed -	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO	BRAF positive 22-44%

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
								Transitional Cell Carcinoma - Therapy Only	AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	urethra extending into bladder neck	19	No	Lapatinib		0	0	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO AND/OR Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO	
Transitional Cell Carcinoma	Urethra	387	Yes	Lapatinib		0	0	BRAF: Mutation - V595E (Transitional Cell Carcinoma),ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO	+
Transitional Cell Carcinoma	Bladder, lungs, neck	18	No			0		ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (EGFR/ERBB2 inhibitor) - 5-	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
									10 mg/kg/day PO	
Transitional Cell Carcinoma	Bladder	51	Yes	Trametinib	yes	1	0	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	bladder, prostate	44	No	Meloxicam, Trametinib		0	4	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2/EGFR inhibitor) - 5-10 mg/kg/day PO	+
Transitional Cell Carcinoma	Bladder / trigonal area	27	No	Lapatinib	no	0	0	BRAF	Trametinib (0.02 mg/kg/day)	+
Transitional Cell Carcinoma	Bladder and suspected prostate	112	No	Trametinib	yes	1	10			+
Transitional Cell Carcinoma	Bladder	134	No	Lapatinib, Trametinib	no	0	7			+
Transitional Cell Carcinoma	Trigone of bladder blcoking right ureter	21	No	Trametinib	no	0	0			+
Transitional Cell Carcinoma	Bladder	103	No	Trametinib, Lapatinib		0	94			

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	Urethra, Lung	144	Yes	Trametinib	yes	1	14	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2/EGFR inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	Bladder	78	No	Trametinib, Lapatinib, Piroxicam		0	13	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	Left ventral trigone of the bladder	177	No	Trametinib	yes	1	0	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	bladder	99	Yes	Trametinib, Lapatinib		0	7	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation	Lapatinib (ERBB2/EGFR inhibitor) - 5-10 mg/kg/day PO	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
								- V595E (Transitional Cell Carcinoma)	AND/OR Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO	
Transitional Cell Carcinoma	prostate +/- bladder	20	No	Trametinib		0	0	ERBB2: Overexpressed - CST, BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	bladder wall		No			0		ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	Prostate	58	No	Trametinib, Lapatinib	unknown	0	46			
Transitional Cell Carcinoma	Distal bladder, urethra and prostate	21	No	Trametinib	no	0	0			+
Transitional Cell Carcinoma	urinary bladder	398	No	Trametinib, Lapatinib	no	0	273			+

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma		162	No	Trametinib, Lapatinib	no	0	52			+
Transitional Cell Carcinoma	Prostate	275	No	Lapatinib	no	0	256			-
Transitional Cell Carcinoma	Prostate	75	No	Lapatinib	yes	1	49			+
Transitional Cell Carcinoma	Urethral, vaginal, lymph node & peri-rectal metastasis	72	No	Lapatinib, Trametinib	yes	1	3	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	bladder	47	No	Trametinib, Lapatinib	no	0	33	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma		45	No	Trametinib	yes	1	42	BRAF: Mutation - V595E (Transitional Cell Carcinoma),ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
									(ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	bladder	179	No	Lapatinib, Trametinib	no	0	148	BRAF Mutation	Trametinib 0.3-0.45 mg/m2/day PO	+
Transitional Cell Carcinoma	bladder	124	No	Piroxicam, Lapatinib	no	0	96	BRAF Mutation	Trametinib (0.02 mg/kg/day)	+
Transitional Cell Carcinoma	bladder	329	No	Lapatinib, Trametinib	no	0	321			+
Transitional Cell Carcinoma	Urethra	549	No	Lapatinib, Trametinib	yes	1	147			+
Transitional Cell Carcinoma	Bladder	585	No	Lapatinib, Trametinib	yes	1	134			+
Transitional Cell Carcinoma	Urinary bladder	1160	Yes	Trametinib, Lapatinib	yes	1	231			
Transitional Cell Carcinoma		535	No	Lapatinib, Trametinib	no	0	486			+
Transitional Cell Carcinoma		535	No	Lapatinib, Trametinib	no	0	486			+
Transitional Cell Carcinoma	Bladder	532	No	Lapatinib, Trametinib	yes	1	452			+
Transitional Cell Carcinoma	Bladder	488	No	Lapatinib, Carprofen, Trametinib	no	0	479			
Transitional Cell Carcinoma	Bladder and probable urethra	1217	Yes	Lapatinib, Trametinib	yes	1	358			+
Transitional Cell Carcinoma	Proximal urethra/urinary bladder, L inguinal lymph node	220	No	Trametinib, Lapatinib	yes	1	45			

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	Bladder	511	No	Trametinib	yes	1	399			+
Transitional Cell Carcinoma	urethral bladder/trigone	1042	No	Trametinib	yes	1	343			+
Transitional Cell Carcinoma	Trigone	357	Yes	Lapatinib, Trametinib	yes	1	84			
Transitional Cell Carcinoma	Bladder	75	No	Trametinib	unknown	0	48			+
Transitional Cell Carcinoma	Urinary Bladder	302	No	Lapatinib, Trametinib	yes	1	63			No BRAF test done
Transitional Cell Carcinoma	bladder	221	No	Trametinib, Lapatinib, Sorafenib	no	0	140			+
Transitional Cell Carcinoma	Bladder/urethra	165	Yes	Lapatinib	yes	1	119			+
Transitional Cell Carcinoma	urinary bladder	998	Yes	Lapatinib, Trametinib	yes	1	264			+
Transitional Cell Carcinoma	Bladder	485	No	Lapatinib, Trametinib	yes	1	244			
Transitional Cell Carcinoma	Apical mural margin mass into the urinary bladder lumen	436	No	Lapatinib, Trametinib	no	0	371			+
Transitional Cell Carcinoma	Urethra	399	No	Trametinib	no	0	356			+
Transitional Cell Carcinoma	Urethra	399	No	Trametinib	no	0	356			
Transitional Cell Carcinoma	Bladder	270	No	Lapatinib, Trametinib	yes	1	209			+

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma		341	No	Trametinib, Lapatinib	no	0	251			+
Transitional Cell Carcinoma	Bladder; Prostate; Urethra	328	Yes	Lapatinib, Trametinib	no	0	181			+
Transitional Cell Carcinoma	bladder	522	No	Lapatinib	yes	1	136			+
Transitional cell carcinoma	Bladder apex	501	No	Trametinib, Lapatinib, Rapamycin	yes	1	297			+
Transitional Cell Carcinoma	Urethra	74	Yes	Trametinib, Lapatinib	yes	1	0			No BRAF test done
Transitional Cell Carcinoma		126	No	Trametinib, Lapatinib	no	0	102			No BRAF test done
Transitional Cell Carcinoma	Urinary Bladder	228	No	Trametinib, Piroxicam, Lapatinib	no	0	208			No BRAF test done
Transitional Cell Carcinoma		312	No	Trametinib	no	0	135			+
Transitional Cell Carcinoma	bladder apex	762	No	Trametinib, Lapatinib	no	0	240			
Transitional Cell Carcinoma	bladder	289	Yes	Trametinib, Lapatinib	yes	1	263			+
Transitional Cell Carcinoma	Bladder	684	No	Trametinib		0	287			
Transitional Cell Carcinoma	Bladder	684	No	Trametinib	no	0	287			+
Transitional Cell Carcinoma	Prostate	396	Yes	Trametinib	yes	1	183			+

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	trigonal bladder	270	No	Trametinib, Lapatinib	no	0	224			+
Transitional Cell Carcinoma	urethra, lymph nodes	419	No	Trametinib, Lapatinib	yes	1	43			+
Transitional Cell Carcinoma	Bladder	172	No	Trametinib, Lapatinib	no	0	93			+
Transitional Cell Carcinoma	Bladder	148	No	Lapatinib, Trametinib	no	0	130			+
Transitional Cell Carcinoma	Bladder, proximal urethra	160	No	Trametinib	yes	1	28			+
Transitional Cell Carcinoma	urethra	250	Yes	Lapatinib, Trametinib	no	0	169			-
Transitional Cell Carcinoma	Bladder	267	No	Lapatinib, Trametinib	yes	1	3			+
Transitional Cell Carcinoma	Prostate	371	Yes	Trametinib, Lapatinib, Toceranib	yes	1	137			No BRAF test done
Transitional Cell Carcinoma		707	No	Trametinib, Lapatinib	yes	1	237			+
Transitional Cell Carcinoma	Bladder	204	No	Lapatinib	yes	1	31			+
Transitional Cell Carcinoma	bladder	45	No	Trametinib, Lapatinib	yes	1	26			+
Transitional Cell Carcinoma	Bladder	568	Yes	Lapatinib, Trametinib	yes	1	153			+
Transitional Cell Carcinoma	Bladder	106	No	Lapatinib, Trametinib	unknown	0	96			+

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	Bladder	266	No	Lapatinib	no	0	205			No BRAF test done
Transitional Cell Carcinoma	SUSPECT BLADDER	206	No	Lapatinib, Trametinib	no	0	203			-
Transitional Cell Carcinoma	Bladder	485	No	Trametinib, Lapatinib	yes	1	244			
Transitional Cell Carcinoma	Bladder, proximal urethra	467	No	Trametinib	yes	1	199			+
Transitional Cell Carcinoma	bladder	451	No	Trametinib, Lapatinib, Rapamycin	yes	1	99			+
Transitional Cell Carcinoma	trigone and extra-urethral mass in area of uterine stump	99	No	Trametinib	no	0	92			+
Transitional Cell Carcinoma	Bladder	632	No	Lapatinib, Trametinib	yes	1	219			+
Transitional Cell Carcinoma	urethra	138	No	Trametinib	yes	1	0			+
Transitional Cell Carcinoma	cranioventral bladder	305	No	Lapatinib	no	0	17			+
Transitional Cell Carcinoma	Bladder	386	No	Lapatinib, Trametinib	yes	1	202			+
Transitional Cell Carcinoma	Bladder, trigone	371	No	Trametinib, Lapatinib	no	0	94			+
Transitional Cell Carcinoma		194	No	Lapatinib, Trametinib	no	0	189			+
Transitional Cell Carcinoma	Urinary bladder	165	No	Trametinib	no	0	150			+

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	pelvic urethra	126	No	Trametinib, Lapatinib	no	0	112			
Transitional Cell Carcinoma		265	No	Lapatinib, Trametinib	yes	1	103			-
Transitional Cell Carcinoma	prostate and bladder	214	No	Trametinib, Lapatinib	yes	1	153			+
Transitional Cell Carcinoma	trigonal region	94	No	Trametinib, Lapatinib	no	0	68			+
Transitional Cell Carcinoma		580	No	Trametinib, Lapatinib	yes	1	76			+
Transitional Cell Carcinoma		208	Yes	Trametinib, Lapatinib	yes	1	86			+
Transitional Cell Carcinoma		146	No	Trametinib, Lapatinib	yes	1	117			+
Transitional Cell Carcinoma	bladder (excised)	86	No			0				
Transitional Cell Carcinoma	bladder (excised)	86	No			0		ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only MEK1/2: Overexpressed - CST,BRAF: Mutation - V595E (Transitional Cell Carcinoma),EGFR: Overexpressed - CST	1. Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO	
Transitional Cell Carcinoma	Bladder and Urethra	390	No	Trametinib, Lapatinib	yes	1	40			

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	bladder	452	No	Lapatinib, Trametinib	yes	1	99		1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO	No BRAF test done
Transitional Cell Carcinoma	Urinary Bladder Mass	130	No	Trametinib, Lapatinib		0	105			+
Transitional Cell Carcinoma	Apex and dorsal bladder wall	158	No	Trametinib	no	0	51			+
Transitional Cell Carcinoma	Bladder	265	No	Trametinib, Lapatinib	no	0	90			+
Transitional Cell Carcinoma	urinary bladder	94	No	Trametinib, Lapatinib	no	0	66			
Transitional Cell Carcinoma	Bladder, Lungs	229	No	Lapatinib, Trametinib	yes	1	100			+
Transitional Cell Carcinoma	Bladder trigone tumor	97	Yes	Trametinib, Lapatinib	no	0	90			+
Transitional Cell Carcinoma		194	Yes	Lapatinib, Trametinib	yes	1	74			
Transitional Cell Carcinoma	apical urinary bladder	64	No		no	0				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
Transitional Cell Carcinoma	Urethra	170	No	Trametinib, Lapatinib	yes	1	63	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	urethra/trigone region of bladder	54	Yes	Lapatinib, Trametinib		0	35	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation - V595E (Transitional Cell Carcinoma)	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	Bladder and Prostate	61	No	Trametinib, Lapatinib	no	0	34	BRAF: Mutation - V595E (Transitional Cell Carcinoma),ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	Prostate	42	Yes	Trametinib, Lapatinib		0	33	ERBB2: Overexpressed - Transitional Cell Carcinoma - Therapy Only BRAF: Mutation	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	CST Alterations	CST Potential Initial Clinical Approach	BRAF Status
								- V595E (Transitional Cell Carcinoma)	AND/OR Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO	
Transitional Cell Carcinoma	Bladder	287	Yes	Trametinib	yes	1	100			+
Transitional Cell Carcinoma	Apex of the bladder	861	Yes	Lapatinib, Trametinib	yes	1	114			+
Transitional Cell Carcinoma	Vaginal Mass	208	No	Trametinib, Lapatinib	yes	1	32			
Transitional Cell Carcinoma	Urethra	431	Yes	Trametinib	yes	1	19			
Transitional Cell Carcinoma	Bladder	234	No	Trametinib, Lapatinib	unknown	0	209			-
Transitional Cell Carcinoma	Bladder	234	No	Trametinib, Lapatinib		0	209			
Transitional Cell Carcinoma	Prostatic urethra	235	No	Trametinib, Lapatinib	unknown	0	213			+
Transitional Cell Carcinoma	Trigonal mass, urethral thickening	169	No	Trametinib, Lapatinib	unknown	0	140			+
Transitional Cell Carcinoma	Bladder	231	Yes	Trametinib, Lapatinib	yes	1	97			
Transitional Cell Carcinoma	Bladder, Abdomen, Colon	372	No	Trametinib, Lapatinib, Vorinostat	no	0	342			-

Table 13: Treatment of Thyroid Carcinoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Genes over expressed	DNA Mutations	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on targeted drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Potential Initial Clinical Approach
Thyroid Carcinoma	Neck (left-side)		No				no	0		JAK3, CREBBP	7 Actionable Findings: CDK4, ERRB2, JAK1, MEK1/2, MET, SRC, mTOR 13 Additional Finding of Importance: AKT, BCL6, BCL-XL, CCND1, GLUT1, HIF1a, MDM2, RAS/RAF, VEGF, ERCC1/2, MGMT, PGP, RRM1/2	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Lapatinib (EGFR, ERBB2 inhibitor) - 5-10 mg/kg/day PO 6. Apoquel (JAK1 inhibitor) - dose per label 7. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 8. Potential sensitivity to platin based and alkylating agents.	1. Canine single nucleotide polymorphism (SNP).	
Thyroid Carcinoma	Left Thyroid Gland	34	No				yes	1		5 Additional Findings of Importance: BRCA2(2), KMT2C,	4 Actionable Findings: CDK4, ERBB2, MEK1/2, SRC 15 Additional Findings	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO 3. Trametinib (MEK inhibitor) -	1. Tumor suppressor gene (BRCA2) 2. Commonly altered gene family in human malignancies (KMT) 3. Previously	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Genes over expressed	DNA Mutations	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on targeted drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Potential Initial Clinical Approach
										IDH1, ROS1	of Importance: AKT, BCL-XL, CCND1, FGFR1, HIF1a, JAK1, MDM2, NR3C1, RAS/RAF, VEGF, BRCA1/2, ERCC1/2, MGMT, PGP, RRM1/2	0.02-0.03 mg/kg/day PO 4. Potential therapeutic benefit of glucocorticoids 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor sensitivity to gemcitabine and/or alkylating agents	identified canine single nucleotide polymorphism (SNP)	
Thyroid Carcinoma	Thyroid	1007	Yes	KIT, MEK, BCL2, BRAF, HER2, MDM2, MGMT, MYC, ERCC1,	EGFR, NOTCH1		yes	1						Lapatinib, Secondary:Trametinib, Dabrafenib Palladia 65mg - 1 cap MWF
Thyroid Carcinoma	left caudal ventral cervical region	330	No			Trametinib	no	0	294	1 Actionable Finding: SETD2 1 Additional Finding of Importance: BRCA2	2 Actionable Findings: CDK4, EGFR, MEK1 7 Additional Findings of Importance: AKT, CCND1, COX2, HIF1a, MDM2,	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Potential therapeutic benefit of non-steroidal anti-inflammatory	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Tumor suppressor gene (BRCA2)	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Genes over expressed	DNA Mutations	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on targeted drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Potential Initial Clinical Approach
											RET, VEGF	drugs (NSAIDs) 5. Biomarkers associated with generalized chemoresistance including potential resistance doxorubicin.		
Thyroid Carcinoma	Thyroid metastatic to retropharyngeal LN at time of dx Jan 2017, met to spleen/liver April 2019	1213	Yes				yes	1	90	9 Additional Findings: BRCA 2(2), FLT3, BRCA 1(4), MET, NOTCH1			1. Potential sensitivity to platin based agents (BRCA2) 2. Tyrosin-kinase receptor (FLT3) 3. Canine single nucleotide polymorphism (SNP).	1. Lapatinib (EGFR/ERB B2 inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO
Thyroid Carcinoma	Thyroid metastatic to retropharyngeal LN at time of dx Jan 2017	1213	Yes			Trametinib, Lapatinib	yes	1	90	9 Additional Findings: BRCA 2(2), FLT3, BRCA 1(4), MET, NOTCH1			1. Potential sensitivity to platin based agents (BRCA2) 2. Tyrosin-kinase receptor (FLT3) 3. Canine single nucleotide polymorphism (SNP).	1. Lapatinib (EGFR/ERB B2 inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Dasatinib (SRC

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Genes over expressed	DNA Mutations	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on targeted drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Potential Initial Clinical Approach
	, met to splen/liver April 2019													inhibitor) - 0.5-0.7 mg/kg/every other day PO
Thyroid Carcinoma	Right Thyroid	101	No					0		2 Additional Findings: CREBBP, NOTCH1			1. Feature of malignant transformation (CREBBP) - consider Vorinostat (HDACi) - 30 mg/kg/every other day PO 2. Canine single nucleotide polymorphism (SNP).	
Thyroid Carcinoma	ventral neck	149	No			Trametinib, Rapamycin	no	0	56					
Thyroid Carcinoma	Cervical, lungs	545	Yes			Trametinib, Lapatinib	yes	1	40					1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Genes over expressed	DNA Mutations	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on targeted drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Potential Initial Clinical Approach
														other day PO
Thyroid Carcinoma	Cervical Mass	1076	No			Rapamycin, Imatinib	yes	1	342	8 Additional Findings of Importance: ATRX, BRCA1 (3), JAK3, KMT2C, NOTCH1, ROS1	5 Actionable Findings: CDK4, EGFR, KDR, MEK1/2, mTOR 9 Additional Findings of Importance: BCL2, CCND1, COX2, MDM2, PGP, RET, VEGF, BRCA1/2, ERCC1/2, MGMT	1. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO 6. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 7. Potential tumor resistance to drugs affected by efflux (PGP) 8. Potential tumor sensitivity to platinum based and alkylating agents (low ERCC1/2 and MGMT). 9. Potential therapeutic benefit from non-steroidal anti-inflammatory drugs (NSAIDs).	1. Mutation of well described tumor suppressor (BRCA1). 2. Commonly altered gene family in human malignancy (KMT). 3. Canine single nucleotide polymorphisms (SNPs).	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Genes over expressed	DNA Mutations	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on targeted drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Potential Initial Clinical Approach
Thyroid Carcinoma	thyroid & retropharyngeal lymph node	236	No	KIT, MEK, BCL2	ARID1A, KMT2C		unknown	0						Palladia & Trametinib Palladia 75mg - 1 cap MWF

Table 14: Treatment of T Cell Lymphoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
T-cell Lymphoma	Mediastinum	80	No	Trametinib, Rapamycin, Vorinostat	yes	1	3				
T-cell Lymphoma	Intestinal	293	Yes	Vorinostat		0	0				
T-cell Lymphoma	multicentric	126	No	Trametinib, Vorinostat, Apoquel	yes	1	72				
T-cell Lymphoma	Left Rostral Upper Lip	71	No	Apoquel, Trametinib, Rapamycin, Dasatinib	yes	1	44	2 Actionable Findings: mTOR, PTEN 1 Additional Finding of Importance: IDH1	3 Actionable Findings: CDK4, JAK1, MEK2	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Apoquel (JAK inhibitor) - dose per label 3. Dasatinib (CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Canine single nucleotide polymorphism (SNP)
T-cell lymphoma	mandibular lymph node, gums, vulva, foot pads, ventral abdomen	146	No		yes	1		3 Additional Findings of Importance: KMT2C, P53, BRAF	4 Actionable Findings: CDK4, JAK1, MEK1/2 6 Additional Findings of Importance: AKT, BCL2, COX2, JAK2, RRM2, STAT1	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Apoquel (JAK inhibitor) - dose per label 3. Dasatinib - 0.5-0.7 mg/kg/every other day PO 4. Potential therapeutic	1. Commonly altered gene family in human malignancies. 2. Mutation of well described tumor suppressor gene (P53). 3. Canine SNP (BRAF)

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Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										benefit of NSAIDs. 5. Potential intracellular signaling via JAK/STAT pathway. 6. Potential tumor resistance to gemcitabine. 7. Potential therapeutic sensitivity to alkylating agents and platinum based therapies.	
T-cell Lymphoma	Jejunum & Duodenum	117	No		yes	1		2 Actionable Findings: NOTCH1, JAK1 5 Additional Findings of Importance: ATRX, JAK3, KMT2C, ROS1, NTRX3	1 Actionable Findings: MEK 6 Additional Findings of Importance: CCND1, COX2, MDM2, PGP, RRM2, PTEN	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 3. Potential tumor resistance to gemcitabine, alkylating agents and/or platin based agents 4. Biomarker associated with a highly proliferative malignancy	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Oclacitinib (JAK inhibitor) - dose per label 3. Tumor suppressor gene in sarcoma (ATRX) 4. Cytokine receptor-mediated intracellular signal (JAK1/JAK3) 5. Commonly altered gene family in human malignancies (KMT) 6. Tyrosine kinase insulin receptor genes (ROS1) 7. Previously identified canine single nucleotide polymorphism (SNP)

Table 15: Squamous Cell Carcinoma

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer [illegible]	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Squamous Cell Carcinoma	Right acetabulum	75	No	no	0				ROS1: Mutation (SNP) - p.Gly1112Ser,KMT2D: Mutation -					

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
									p.Met1832Ile,KMT2D: Mutation - p.Val4565Ala,FLT3: Mutation (SNP) - p.His700Arg					
Squamous Cell Carcinoma	left tonsil	60	No	no	0	22	JAK3: Mutation - p.Arg925Cys			Trametinib				
Squamous Cell Carcinoma	left labial commissure	291	No	no	0	203	PDGFRβ: Inframe Insertion - Ala1064_Asp1065insAlaAsp,FLT3: Mutation - p.Thr142Ile,SETD2: Mutation - Gly594Asp		NOTCH1: Mutation (SNP) - p.Val2035Ile,NTRK1: Mutation (SNP) - p.Arg220Gln,PDGFRβ: Mutation (SNP) - p.Arg705Cys,KMT2D: Mutation - p.Pro895_Arg904del,KMT2D: Mutation - p.Gln746Arg,BRCA2: Mutation - p.Met3332_Lys3333insIleLys,PTPRT: Mutation - p.Leu748Ile,ARID1A: Mutation - p.Ala822Thr,VEGFβ: Mutation (SNP) - p.Thr195Ala,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,KMT2C: Mutation - p.Gln3726_Pro3727fs				
Squamous Cell Carcinoma	Tonsillar region, retropharyngeal	630	Yes	yes	1		SETD2: Mutation - Gly594Asp,PDGFRβ: Inframe Insertion - Ala1064_Asp1065insAlaAsp,NOT		ROS1: Mutation (SNP) - p.Thr2260Met,MET: Mutation (SNP) - p.Asp583Asn,CREBBP: Mutation - p.	Trametinib, Toceranib, Rapamycin				

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
	lymph node						CH1: Mutation - p.Val1742Leu,PTEN: Mutation - p.Asp25fs		Pro2046_Gln2047del					
Squamous Cell Carcinoma	Primary site unknown; pulmonary metastasis, SQ	131	No	yes	1	86	K-RAS: Mutation - p.Gly12Arg	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed	KMT2C: Mutation (SNP) - p.His325Tyr,ROS1: Mutation (SNP) - p.Ile133Val,BRAF: Mutation (SNP) - p.Ile322Val	Rapamycin, Trametinib				
Squamous Cell Carcinoma - 5-15 mm margins	left mandibular cheek carcinoma - 5-15 mm margins	760	No	yes	1		P53: Mutation - p.Gly106fs,KMT2D: Mutation - p.Ala3904Thr,FLT3: Mutation (SNP) - p.Thr142Ile	PGP: Underexpressed ,MGMT: Underexpressed ,BRCA1/2: Underexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,BCL6:			3 Additional Findings of Importance: FLT3, KMT2D, P53	6 Actionable Findings: CDK4, EGFR, JAK1, MEK1/2, MYC, PDGFR 10 Additional Findings of Importance: AKT, BCL6, CCND1, HIF1a, JAK2, MDM2, RAS/RAF,	1. Lapatinib (EGFR/ERBB 2 inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO	1. Mutation of well described tumor suppressor gene (P53). 2. Commonly altered gene family in human malignancies (KMT). 3. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								Overexpressed ,AKT: Overexpressed				BRCA1/2, MGMT, PGP	5. Apoquel (JAK inhibitor) - dose per label 6. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 7. Biomarkers associated with generalized chemoresistance and an aggressive phenotype. 8. Potential tumor resistance to doxorubicin (low TOP2A) and sensitivity to platins and alkylating agents (low ERCC1/2 and MGMT).	
Squamous Cell Carcinoma	Left Tonsil	55	No	no	0	0		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,STAT1:	ROS1: Mutation (SNP) - p.Thr2260Met,ATRX : Mutation - p.Lys844Asn,CDK4: Mutation - p.Cys78Ser	Lapatinib	1 Actionable Findings: CDK4 2 Additional Findings of Importance: ATRX, ROS1	7 Actionable Findings: CDK4, EGFR, ERBB2, JAK1, MEK2, MET, MYC 14 Additional Findings of Importance: AKT, BCL-	1. Lapatinib (ERBB2, EGFR inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Dasatinib (SRC inhibitor)	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Mutation of tumor suppressor gene (ATRX). 3. Canine

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								Overexpressed ,RRM1/2: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed				XL, COX2, GLUT1, HIF1a, MDM2, RAS/RAF, RRM1/2, STAT1, TOP2A, BRCA1/2, ERCC1/2, MGMT, PGP	- 0.5-0.7 mg/kg/every other day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Apoquel (JAK inhibitor) - dose per label 6. Potential tumor sensitivity to platinum based agents (low ERCC1/2 and BRCA1/2), alkylating agents (low MGMT), antracycline (high TOP2A), and resistance to gemcitabine (high RRM1/2) 7. Genes related to chemotherapy and tyrosine kinase resistance are expressed in this tumors 8. High expression of COX-2 suggest	single nucleotide polymorphisms (SNPs).

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
													benefits of NSAIDs	
Squamous Cell Carcinoma	Right lateral hard palate	350	No	no	0	115		RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,ERCC2: Overexpressed ,CCND1: Overexpressed ,BCL6: Overexpressed	NOTCH1: Mutation (SNP) - p.Ala2121Thr,ROS1: Mutation - p.Gly236Ser,MIEN1: Mutation - p.Arg94Gln,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,JAK2: Mutation - p.Glu877Lys,EGFR: Mutation (SNP) - p.Arg202Gln	Trametinib, Piroxicam, Lapatinib, Dasatinib, Rapamycin	6 Additional Findings of Importance: EGFR, JAK2, KMT2C, MIEN1, ROS1, NOTCH1	4 Actionable Findings: CDK4, EGFR, MYC, PDGFR 8 Additional Findings of Importance: BCL6, CCND1, ERCC2, GLUT1, HIF1a, MGMT, PGP, RRM1/2	1. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 2. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 4. Palladia (PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 5. Vorinostat (MYC inhibitor) - 30 mg/kg/every other day PO 6. Biomarkers associated with generalized chemo-resistance. 7. Potential tumor sensitivity to alkylating agents and/or gemcitabine.	1. Mutation of epidermal growth factor receptor (EGFR). 2. Tyrosine kinase involved in cytokine intracellular signal transduction (JAK2). 3. Commonly altered gene family in human malignancies (KMT2C) 4. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Squamous Cell Carcinoma	Right tonsil and right medial retropharyngeal lymph node	138	No	no	0	63	ATM: Mutation - p.Glu2815fs	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,STAT1: Overexpressed ,PTEN: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,AKT: Overexpressed	PDGFRβ: Mutation (SNP) - p.Arg705Cys,KMT2C: Mutation (SNP) - p.His906Tyr,IDH1: Mutation (SNP) - p.Gly175Ser,ARID1A: Mutation - p.Ala822Thr	Vorinostat, Trametinib	1 Actionable Finding: ATM 4 Additional Findings of Importance: ARID1A, IDH1, KMT2C, PDGFRβ	3 Actionable Findings: CDK4, JAK1, MEK1 12 Additional Findings of Importance: AKT, GLUT1, HIF1a, JAK2, MDM2, STAT1, TOP2A, PTEN, BRCA1/2, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Dasatinib (CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Apoquel (JAK inhibitor)- dose per label 4. Biomarkers associated with generalized with chemo-resistance 5. Potential tumor sensitivity to alkylating and platinum based agents.	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Member of the SWI/SNF family (ARID1A). 3. Previously identified canine single nucleotide polymorphism (SNP).
Squamous Cell Carcinoma	lateral right side of tongue	149	No	yes	1	110		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,STAT1: Overexpressed	ROS1: Mutation (SNP) - p.Ile133Val,MET: Mutation (SNP) - p.Asn870Lys,RET: Mutation - p.Asn870Lys,PARP 1: Mutation - p.Thr148Ala,P53: Mutation - p.Leu46fs,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	Lapatinib, Trametinib	6 Additional Findings of Importance: KMT2C, P53, PARP1, RET, MET, ROS1	4 Actionable Findings: EGFR, MEK2, MET, MYC 10 Additional Findings of Importance: AKT, HIF1a, PTEN, RRM2, STAT1, VEGF,	1. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Vorinostat (MYC inhibitor) - 30 mg/kg/every	1. Commonly altered gene family in human malignancies (KMT) 2. Mutation of well described tumor suppressor gene (P53) 3. Mutation

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								ed ,RRM2: Overexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,AKT: Overexpressed				BRCA1/2, ERCC1/2, MGMT, PGP	other day PO 4. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 5. Potential tumor sensitivity to alkylating agents and/or platin based chemotherapy . 6. Potential tumor resistance to gemcitabine. 7. Biomarkers associated with generalized chemo-resistance.	in DNA damage repair gene (PARP1) 4. Tyrosine kinase receptor mutation (RET) 5. Canine single nucleotide polymorphism (SNP)
Squamous Cell Carcinoma	maxillary mass, invasive to nasal cavity	252	No	yes	1	74		MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed ,STAT1: Overexpressed ,RRM2: Overexpressed ,RAS/RAF:	NOTCH1: Mutation (SNP) - p.Thr14Lys,KMT2C: Mutation (SNP) - p.Pro4236Leu,FLT3: Mutation - p.Val186Ileu,ROS1: Mutation - p.Thr335Lys,PARP1: Mutation (SNP) - p.Ala451Glu,P53: Mutation - p.Arg147Cys,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FLT3:	Trametinib, Lapatinib	8 Additional Findings of Importance: FLT3(2), KMT2C(2), P53, PARP1, ROS1, NOTCH1	4 Actionable Findings: CDK4, EGFR, MEK1/2, MYC 18 Additional Findings of Importance: AKT, CDKN2A, COX2, DHFR, GLUT1, HIF1a, JAK1, JAK2, MDM2,	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Vorinostat (HDAC inhibitor) - 30	1. Tyrosin-kinase receptor (FLT3) 2. Commonly altered gene family in human malignancies (KMT) 3. Mutation of well described tumor suppressor gene (P53) 4. Gene of

Tumor type	Tumor Location	Total Survival time	Radiation	Previous cancer	Traditional Therapy Refractory (yes=1, no =0)	Total Days on FC Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								Overexpressed ,PTEN: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,DHFR: Overexpressed ,COX2: Overexpressed ,CDKN2A: Overexpressed ,AKT: Overexpressed				PTEN, RAS/RAF, RRM2, STAT1, TOP2A, VEGF, BRCA1/2, ERCC1/2, MGMT	mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 7. Potential tumor resistance to gemcitabine 8. Potential tumor resistance to doxorubicin that may be re-sensitized with Rapamycin. 9. Potential tumor sensitivity to methotrexate, 5'FU and/or alkylating agents	DNA damage repair (PARP1) 5. Tyrosine kinase insulin receptor (ROS1) 6. Previously identified canine single nucleotide polymorphism (SNP)
Squamous Cell Carcinoma	tonsillar and retropharyngeal node	237	No	yes	1	191			Mutation - p.Asp748Asn	Toceranib, Imatinib				

Table 16: Treatment of Soft Tissue Sarcoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Soft Tissue Sarcoma	Right thorax	39	Y	Dasatinib, Rapamycin	Y	1	3	Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO AND Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO	MEK1: Overexpressed ,CDK4: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,PTEN: Overexpressed ,CDKN2A: Overexpressed ,AKT: Overexpressed	BRCA1: Mutation (SNP) - p.Gly192Ser,ABL1: Mutation (SNP) - p.Leu830Phe,ROS1: Mutation - p.Leu2013Met,ROS1: Mutation - p.Arg56Gln,P53: Mutation - p.Gln182fs,PDGFRβ: Mutation (SNP) - p.Arg705Cys,BRCA2: Mutation (SNP) - p.Asn2929Asp,BRCA1: Mutation - p.Gly264Asp	8 Additional Findings of Importance: BRCA1(2), BRCA2, PDGFRβ, P53, ROS1(2), ABL1	2 Actionable Findings: CDK4, MEK1 10 Additional Findings of Importance: AKT, CDKN2A, PTEN, RRM2, TOP2A, TYMS, BRCA1/2, ERCC1/2, MGMT, PGP	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Potential resistance to gemcitabine. 4. Potential tumor sensitivity to anthracyclines, 5-FU, alkylating agents and/or platin based chemotherapy.	1. Tumor suppressor genes (BRCA1, BRCA2) 2. Tyrosine kinase insulin receptor gene (ROS1) 3. Mutation of well described tumor suppressor gene (P53) 4. Canine single nucleotide polymorphism (SNP)
Soft Tissue Sarcoma	Right orbit extend	79	N	Trametinib, Rapamycin	N	0	23	Trametinib (MEK inhibitor) -	PDGFR: Overexpressed ,MYC:	SETD2: Mutation -	TOP2A: Overexpressed ,STAT1:	PDGFRβ: Mutation (SNP) - p.Arg705Cys,MET	2 Actionable	3 Actionable	1. Trametinib (MEK	1. Dasatinib (SRC

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
	ing to oral cavity							0.02-0.03 mg/kg/day PO AND Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO	Overexpressed ,MEK1/2: Overexpressed - CST	p.Arg1060Cys	Overexpressed ,RAS/RAF: Overexpressed ,PTEN: Overexpressed ,PIK3CA: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,FGFR2: Overexpressed ,FGFR1: Overexpressed ,BCL2: Overexpressed ,AKT: Overexpressed	: Mutation (SNP) - p.Asp583Asn,MET : Mutation (SNP) - p.Gly937Ser,VEGFB: Mutation - p.His151Arg,NTRK1: Mutation - p.Glu535Lys,BRCA2: Mutation - p.Asn636_Cys637fs,CDK4: Mutation - p.Cys78Ser	Finding s: CDK4, SETD2 6 Additional Finding s: BRCA2, NTRK1, VEGFB, MET(2), PDGFRβ	Finding s: MEK1/2, MYC, PDGFR , 11 Additional Finding s of Importance: AKT, BCL2, FGFR1 , FGFR2 , JAK1, JAK2, PIK3CA, PTEN, RAS/RAF, STAT1, TOP2A	inhibitor) - 0.02-0.03 mg/kg/day PO 2. Toceranib (PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor sensitivity to	inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Tumor supressor gene (BRCA2) 4. Neutrophilic tyrosine receptor kinase (NTRK1) 5. Vascular endothelial growth factor (VEGFB) 6. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															methotrexate and/or doxorubicin.	
Soft Tissue Sarcoma	soft pallet	40	Y		Y	1										
Soft Tissue Sarcoma	L lateral thorax (site of previous amputation for STS)	175	N		N	0						KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,KMT2C: Mutation (SNP) - p.His906Tyr				
Soft Tissue Sarcoma	Ventral thorax	370	Y	Rapamycin, Dasatinib, Trametinib	Y	1	34		PDGFRB: Mutation - p.Glu400Lys			RTP2: Mutation (SNP) - p.His97Tyr,CREBBP: Mutation - p.Pro2046_Gln2047del,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,FGFR3: Mutation - p.Val512_Tyr513fs				
Soft Tissue Sarcoma	Left Axilary	989	Y	Trametinib, Rapamycin	N	0	168	Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2: Overexpressed - CST,EGFR	SETD2: Mutation - p.Tyr1268Phe,NF1: Mutation (SNP) - p.Arg2561Gln,BRAF: Mutation	MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,RAS/RAF: Overexpressed ,NR3C1:	FLT3: Mutation (SNP) - p.Thr142Ile,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation (SNP) - p.Ala1873Thr,P53:				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Soft Tissue Sarcoma	left shoulder	506	N	Trametinib, Rapamycin, Imatinib	N	0	254	Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO	PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,EGFR: Overexpressed	ATM: Mutation - p.Asp711Ala	TOP2A: Overexpressed ,RRM1/2: Overexpressed ,PIK3CA: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed	VEGFB: Mutation (SNP) - Intron variant,MET: Mutation (SNP) - p.Asp583Asn,JAK2: Mutation (SNP) - p.Ile19Val,KMT2C: Mutation - p.3163_3164insAsnLys,P53:	1 Actionable Finding: ATM 1 Additional Finding of Importa	6 Actionable Findings: CDK4, EGFR, JAK1, MEK1/2, PDGFR 6	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Rapamycin (mTOR inhibitor) - 0.1	1. Vorinostat (HDAC inhibitor) - 45 mg/kg/every other day PO 2. Mutation of well-
Soft Tissue Sarcoma	Left Elbow	762	No	Dasatinib, Rapamycin	Y	1	259	Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO	PDGFR: Overexpressed ,mTOR: Overexpressed - CST,MEK1/2: Overexpressed - CST,EGFR: Overexpressed - CST,CDK4: Overexpressed	ATM: Mutation - p.His1144Leu,ATM: Mutation - p.Met1756Thr	MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,E2F1: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	NTRK3: Mutation (SNP) - p.Ser42Asn,MET: Mutation (SNP) - p.Asp583Asn,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,KMT2C: Mutation - p.3163_3164insAsnLys					
									: Overexpressed - CST,CDK4: Overexpressed	- p.Val588Glu (Canine and human hotspot mutation)	Overexpressed ,MDM2: Overexpressed ,CCND1: Overexpressed ,BCL2: Overexpressed ,AKT: Overexpressed	Mutation - p.Glu23* STOP				

Tumor type		
Tumor Location		
Total Survival time (in Days)		
Radiation		
Targeted drugs		
Previous cancer therapy		
Traditional Therapy Refractory (yes=1, no =0)		
Total Days on Targeted Drugs		
Potential Initial Clinical Approach		
Actionable RNA Alterations	sed - CST,CDK4 . . Overexpressed	
Potentially Clinically Significant Findings		
Other RNA Alterations		
Other Potentially Unknown Clinical Significance Findings	Mutation - p.Leu184Arg	
DNA Sequencing Findings	nce: P53	
Gene Expression Findings	Additional Findings of Importance: AKT, BCL-XL, PIK3CA, RRM1/2, TOP2A	
RNA Therapeutic Indications	mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 5. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 6. Potential intracellular signaling through AKT/PI3K/mTOR and MAPK/ERK pathways. 7. Potential tumor sensitivity to anthracycli	
DNA Therapeutic Indications	described tumor suppressor.	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Soft Tissue Sarcoma	Skin	300	Y	Trametinib, Rapamycin, Dasatinib, Apoquel	Y	1	77	Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO AND Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO	JAK1: Overexpressed - CST,CDK4: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,STAT1: Overexpressed ,AKT: Overexpressed	NTRK3: Mutation (SNP) - p.Ser42Asn,JAK2: Mutation (SNP) - p.Ile19Val,RET: Mutation - p.His354Tyr,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Gly59Ser	5 Additional Findings of Importance: CREBBP, KMT2C, RET, JAK2, NTRK3	2 Actionable Findings: CDK4, JAK1 5 Additional Findings of Importance: AKT, STAT1, ERCC1/2, MGMT, PGP	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Apoquel (JAK1 inhibitor) - dose per label 3. Potential tumor sensitivity to alkylating agents and/or platin based chemotherapy.	nes. 8. Potential tumor resistance to gemcitabine.	1. Transcription activating gene (CREBBP) 2. Commonly altered gene family in human malignancies (KMT) 3. Tyrosine kinase receptor activated by GDNF (RET) 4. Previously identified canine single nucleotid

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Soft Tissue Sarcoma	right ventral lateral thorax	85	N	Rapamycin, Trametinib		0	27	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO AND Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO				ATM: Mutation (SNP) - p.Asp711Ala,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	2. Additional Findings: KMT2C, ATM		1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 4. Toceranib (PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every	1. Commonly altered gene family in human malignancies (KMT) 2. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															y other day PO	
Soft Tissue Sarcoma	Left lateral dorsal neck	354	Y		Y	1		Consider traditional chemotherapy (as indicated on this report)				FLT3: Mutation - p.Val186Leu,CDKN2A: Mutation (SNP) - p.Ala89Ser,FLT3: Mutation - p.Asp748Asn,BRCA2: Mutation - p.Pro3213Leu,ATRX: Mutation - p.Arg2076Gln	5 Additional Findings: ATRX, BRCA2, FLT3, CDKN2A, FLT3			1. Tumor suppressor genes (ATRX, BRCA2) - potential benefit from platin-based agents 2. Tyrosine kinase receptor (FLT3) 3. Previously identified canine single nucleotide polymorphism (SNP).
Soft Tissue Sarcoma	caudal abdominal wall	423	N	Lapatinib	Y	1	43	Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO AND/OR Traditional chemotherapy		EGFR: Mutation - p.Gly466Ala		ROS1: Mutation (SNP) - p.Thr2260Met,ROS1: Mutation (SNP) - p.Lys2Arg,BRCA1: Mutation (SNP) - p.Gly192Ser,BRC	1 Actionable Finding s: EGFR 4 Addition			1. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 2. Tumor suppress

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
												A1: Mutation - p.Gly264Asp	al Finding s: BRCA1(2), ROS1(2)			or gene, potential sensitivity to platin based agents (BRCA1) 3. Canine single nucleotide polymorphism (SNP).
Soft Tissue Sarcoma	vertebral canal of L5	281	Y		Y	1		Toceranib (FLT3 inhibitor) - 2.5-3.25 mg/kg/every other day PO		FLT3: Mutation (SNP) - p.His700Arg		VEGFβ: Mutation (SNP) - Intron variant,VEGFβ: Mutation (SNP) - p.Thr195Ala,PDGFRβ: Mutation (SNP) - p.Arg705Cys,NOTCH1: Mutation (SNP) - p.Ser1456Asn,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	1 Actionable Finding s: FLT3 5 Additional Finding s: KMT2C, NOTCH1, PDGFRB, VEGFB (2)			1. Toceranib (FLT3 inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Commonly altered gene family in human malignancies (KMT) 3. Previously identified canine

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Soft Tissue Sarcoma	Inguinal mass	386	N	Dasatinib, Rapamycin	Y	1	0	Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO AND Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO	PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,CDK4: Overexpressed	SETD2: Mutation - p.Pro5Gln	MDM2: Overexpressed ,FGFR2: Overexpressed ,FGFR1: Overexpressed ,E2F1: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,BCL-XL: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed	VEGFC: Mutation - p.Val342Ile,MET: Mutation (SNP) - p.Asp583Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser,BRCA1: Mutation (SNP) - p.Gly192Ser,SMARCA4: Mutation - p.Pro263_Gly264fs,KMT2D: Mutation - p.Gln746Arg,BRCA2: Mutation (SNP) - p.Asn2929Asp,BRCA1: Mutation - p.Lys42Gln,BRCA1: Mutation - p.Val1230Ile	1 Actionable Finding s: SETD2 9 Additional Findings of Importance: BRCA1(3), BRCA2, KMT2D, SMARCA4, CDKN2A, MET, VEGFC	3 Actionable Findings: CDK4, MEK1/2, PDGFR 9 Additional Findings of Importance: AKT, BCL6, BCL-XL, CCND1, COX2, E2F1, FGFR1, FGFR2, MDM2	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 3. Toceranib (PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 5. Potential therapeutic benefit of	single nucleotide polymorphism (SNP).	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Tumor supressor genes (BRCA1, BRCA2) 3. Commonly altered gene family in human malignancies (KMT) 4. Component of SWI/SNF protein complexes (SMARCA4) 5.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation (Y/N)	Targeted Drugs	Previous cancer therapy (Y/N)	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations
Pulmonary Adenocarcinoma	Right caudal	233	N	Lapatinib		0									ERBB2: Mutation - p.Val659Gl

Table 17: Treatment of Pulmonary Adenocarcinoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potential Initial Clinical Approach	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															non-steroidal anti-inflammatory drugs (NSAIDs). 6. Potential tumor resistance to doxorubicin that may be re-sensitized with rapamycin.	Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation (Y/N)	Targeted Drugs	Previous cancer therapy (Y/N)	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations
	lung lobe														u,K-RAS: Mutation - CST
Pulmonary Adenocarcinoma	Pulmonary	341	N	Lapatinib	y	1									ERBB2: Mutation - p.Val659Glu,PTEN: Mutation - CST,MEK1/2: Overexpressed - CST
Pulmonary Adenocarcinoma	Lung	112	N	Lapatinib	n	0		ERBB2: Mutation - p.Val659Glu, BRCA2: Mutation - p.Met3332Lys		KMT2D: Mutation - p.Gly3926Arg,CREBBP: Mutation - p.Gly59Ser, CDKN2A: Mutation (SNP) - p.Ala89Ser					
Pulmonary Adenocarcinoma	Right middle lung lobe	277	Y	Lapatinib	y	1	MEK1/2: Overexpressed - CST,ERBB2 (HER2/neu): Overexpressed ,EGFR: Overexpressed - CST,CDK4: Overexpressed	ERBB2: Mutation - p.Val659Glu, ATM: Mutation - p.Glu2479Lys,ATM: Mutation - p.Ala2347Thr	PGP: Underexpressed ,MGMT: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,STAT1: Overexpressed ,RRM2: Overexpressed ,MDM2: Overexpressed	ROS1: Mutation (SNP) - p.Arg1606His,NOTCH1: Mutation (SNP) - p.Ser1456As n,KMT2C: Mutation (SNP) - p.His906Tyr, BRCA2: Mutation -	3 Actionable Findings: ATM(2), ERBB2 4 Additional Findings of Importance: BRCA2, KMT2C, NOTCH1, ROS1	4 Actionable Findings: CDK4, EGFR, ERBB2, MEK1/2 13 Additional Findings of Importance: AKT, COX2, GLUT1, HIF1a, JAK1, JAK2, MDM2,	1. Lapatinib (EGFR/ERB B2 inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Dasatinib (SRC inhibitor) -	1. Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Tumor suppressor gene (BRCA2)	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation (Y/N)	Targeted Drugs	Previous cancer therapy (Y/N)	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations
Pulmonary Adenocarcinoma	all lung fields	503	N	Lapatinib, Trametinib		0			ed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed ,AKT: Overexpressed	p.Glu1587Lys		RRM2, STAT1, VEGF, BRCA1/2, MGMT, PGP	0.5-0.7 mg/kg/every other day PO 4. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor resistance to gemcitabine 7. Potential tumor sensitivity to methotrexate and/or alkylating agents	4. Previously identified canine single nucleotide polymorphism (SNP)	
Pulmonary Adenocarcinoma	cranial medastinal mass	849	N	Lapatinib, Trametinib, Rapamycin	y	1		ERBB2: Mutation - p.Val659Glu, NOTCH1: Mutation - p.Val2035Leu		VEGFβ: Mutation (SNP) - p.Thr195Ala, VEGFβ: Mutation					

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation (Y/N)	Targeted Drugs	Previous cancer therapy (Y/N)	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations
										(SNP) - p.Leu146Val, PIK3CA: Mutation - Glu970Lys,C REBBP: Mutation - p. Pro2046_Gln 2047del,KM T2C: Mutation (SNP) - p.His906Tyr, BRCA2: Mutation - p. Cys386Trp,B RCA2: Mutation - p. His143Arg					
Pulmonary Adenocarcinoma	Lung	182	N	Lapatinib, Trametinib		0		NOTCH1: Mutation - p.Ala542Val, ERBB2: Mutation - p.Val659Glu		CDKN2A: Mutation (SNP) - p.Ala89Ser,S MARCA4: Mutation - p.Asp1595Ty r,P53: Mutation - p.Glu275Lys	2 Actionable Findings: ERBB2, NOTCH1 3 Additional Findings of Importance: P53, SMARCA4, CDKN2A		1. Lapatinib (ERBB2/EGFR inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Dasatinib	1. Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Mutation of well described tumor suppressor gene (P53) 4. Component	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation (Y/N)	Targeted Drugs	Previous cancer therapy (Y/N)	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations
													(SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO	of SWI/SNF protein complexes (SMARCA4) 5. Canine single nucleotide polymorphism (SNP).	
Pulmonary Adenocarcinoma	left cranial lung	136	N		y	1		RET: Mutation - p.Ala975Val, ERBB2: Mutation - p.Val659Glu		VEGFβ: Mutation (SNP) - p.Thr195Ala, VEGFβ: Mutation (SNP) - p.Leu146Val, JAK2: Mutation (SNP) - p.Ile19Val,FGFR2IIIC: Mutation - p.Thr368Met ,ALK: Stop Gained - p.Gly1616*				
Pulmonary Adenocarcinoma	primary lung mass	301	N	Trametinib	n	0									
Pulmonary Adenocarcinoma	Right cranial lung lobe, Right third mamm	153	N	Lapatinib	unknown	0									ERBB2: Mutation - p.Val659Glu

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation (Y/N)	Targeted Drugs	Previous cancer therapy (Y/N)	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Unknown Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations
	ary gland nodule														
Pulmonary Adenocarcinoma	Left cranial lung lobe		N		n	0				ROS1: Mutation (SNP) - p.Ile133Val, PARP1: Mutation (SNP) - p.Ala451Glu, JAK2: Mutation (SNP) - p.Ile19Val					
Pulmonary Adenocarcinoma	Lung		N		n	0									
Pulmonary Adenocarcinoma	Intravascular, suspect lung, possibly pleura		N			0									

Table 18: Treatment of Osteosarcoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings
Osteosarcoma	Proximal humerus-has been amputated.	421	Yes		yes	1		PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,ERBB2 (HER2/neu): Overexpressed		MGMT: Underexpressed ,RRM1/2: Overexpressed ,PI3K: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,ERCC2: Overexpressed ,COX2: Overexpressed ,AKT: Overexpressed	
Osteosarcoma	Maxillary	56	No		no	0			NF1: Mutation (SNP) - p.Arg2561Gln,mTOR: Mutation - p.Asp1376Glu		IDH1: Mutation (SNP) - p.Gly175Ser,PDGFRβ: Mutation - p.Glu400Lys,P53: Mutation - p.Ser116Tyr,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,KDR: Mutation - p.Lys797Asn,FLT3: Mutation - p.Ser924Phe,BRCA2: Mutation - p.Thr1425Pro,BRCA2: Mutation - p.Ile103Thr,ALK: Stop Gained - p.Gly1616*
Osteosarcoma	Right 7th rib	43	No		yes	1					
Osteosarcoma	FL proximal radius	42	No		no	0			SETD2: Stop Gained - p.Glu1418*,SETD2: Mutation - Gly594Asp		ROS1: Mutation (SNP) - p.Gly1112Ser,NTRK3: Mutation (SNP) - p.Ser42Asn,NOTCH1: Mutation - p.Asp2089Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser,ROS1: Mutation (SNP) - p.Thr1373Ile,ROS1: Mutation - p.Arg66Gln,PARP1: Mutation - p.Ser340Arg,P53: Mutation - p.Val262Leu,P53:

											Mutation - p.Thr112Met,KIT: Inframe Deletion - p.Leu16del
Osteosarcoma	Distal right radius	27	No			0					
Osteosarcoma	Right pelvic limb	138	No		yes	1			PDGFRα: Mutation - p.Arg696His		ROS1: Mutation (SNP) - p.Arg1606His,MET: Mutation (SNP) - p.Gly937Ser,BRCA2: Mutation - p.Met3332_Lys3333insIleLys,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,P53: Mutation - p.Arg237Gln,CREBBP: Mutation - p.Pro2046_Gln2047del,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation (SNP) - p.Ala1873Thr,BRCA1: Mutation - p.Thr1101Ala,BRCA1: Mutation - p.Gly451Asp
Osteosarcoma	proximal humerus	258	No	Vorinostat, Rapamycin, Meloxicam, Sorafenib, Dasatinib, Crizotinib, Erlotinib	yes	1	183	MYC: Overexpressed ,VEGF: Overexpressed ,PDGF: Overexpressed	MET: Mutation ,mTOR: Mutation - p.Asp1376Glu,EGFR: Mutation - p.Pro236Leu	MDM2: Overexpressed ,ERCC2: Overexpressed ,MGMT: Overexpressed ,COX2: Overexpressed	BRCA2: Inframe Insertion ,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,ROS1: Mutation (SNP) - p.Thr2260Met,ATRX: Mutation - p.Arg210*,CREBBP: Mutation - p.Pro2046_Gln2047del
Osteosarcoma	Right proximal tibia, now pulmonary metastatic disease	222	No		yes	1			NOTCH1: Mutation - p.Val2035Leu,ATM: Mutation - p.His1144Leu,JAK3: Mutation - p.Ser151Pro,KDR: Mutation - p.Ala594Val,P53: Mutation - p.Gly232*		RTP2: Mutation (SNP) - p.His97Tyr,ROS1: Mutation (SNP) - p.Pro2322Ala,BRCA1: Mutation (SNP) - p.Gly192Ser,PARP1: Mutation (SNP) - p.Ala451Glu,BRCA1: Mutation - p.Gly451Asp,NTRK3: Mutation (SNP) - p.Ser42Asn,KMT2C: Mutation (SNP) - p.His906Tyr,ROS1: Mutation - p.Ile1826Val
Osteosarcoma	L proximal humerus	223	No	Dasatinib, Rapamycin	yes	1	63				
Osteosarcoma	maxilla, right	109	No	Dasatinib, Rapamycin	no	0	41	MYC: Overexpressed ,MEK2: Overexpressed ,CDK4: Overexpressed	SETD2: Stop Gained - ARG1426*,SETD2: Mutation - Gly594Asp,PIK3CA: Mutation - P.Glu542Lys	ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,RRM2: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1:	KMT2C: Mutation (SNP) - p.His906Tyr,PTPRT: Mutation - p.Ala288Ser

Osteosarcoma	left sided rib mass and right pleura nodule	189	No	Rapamycin, Dasatinib	yes	1	61	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	NF1: Mutation (SNP) - p.Arg2561Gln	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,PDGF: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,AKT: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,CREBBP: Mutation - p.Arg1291Gln
Osteosarcoma		275	No	Rapamycin, Dasatinib, Trametinib	yes	1	84	SRC: Overexpressed - CST,PDGFR: Overexpressed ,mTOR: Overexpressed - CST,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		MGMT: Underexpressed ,ERCC1/2: Underexpressed ,TOP2A: Overexpressed ,STAT1: Overexpressed ,RRM1/2: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,E2F1: Overexpressed ,CCND1: Overexpressed	FLT3: Mutation (SNP) - p.His700Arg,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation - p.Gly264Asp

Osteosarcoma	Left proximal femur (has a second confirmed OSA at right distal radius)	396	No	Rapamycin, Dasatinib	no	0	30	PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Ile133Val,EGFR: Mutation (SNP) - p.Arg202Gln,RET: Mutation - p.Ala975Val,PDGFRβ: Mutation - p.Glu400Lys
Osteosarcoma	distal right radius	242	No	Dasatinib, Rapamycin	unknown	0	115	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		RRM1/2: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,TYMS: Overexpressed ,PTEN: Overexpressed ,PDGF: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,DHFR: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Ile133Val,VEGFA: Mutation - p.Val210Ala,KMT2D: Mutation - p.Ser744Pro,KMT2D: Mutation - p.Gln746Arg,FGFR3: Mutation (SNP) - p.Arg146Trp,BRCA2: Mutation - p.Glu3000Lys
Osteosarcoma	Left distal femur	81	No	Dasatinib	no	0	10	MEK2: Overexpressed ,CDK4: Overexpressed	PDGFRβ: Mutation - p.Asp384Asn	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed	ABL1: Mutation (SNP) - p.Leu830Phe,ROS1: Mutation (SNP) - p.Pro2322Ala,P53: Mutation - p.Arg145His,KMT2D: Mutation - p.Arg2905His

									,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,TYMS: Overexpressed ,RAF: Overexpressed ,HIF1a: Overexpressed ,COX2: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed	
Osteosarcoma	Mandible, Left	65	No	Trametinib, Rapamycin	no	0	22	MEK1: Overexpressed ,CDK4: Overexpressed	SETD2: Mutation - p.Ala555Pro	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,RRM2: Overexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,FGFR2: Overexpressed ,FGFR1: Overexpressed ,AKT: Overexpressed	CREBBP: Mutation (SNP) - p.Gly2097Ser,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,ABL1: Mutation - p.Gly665Arg
Osteosarcoma	RFL distal radius	154	No		no	0		MYC: Overexpressed ,MEK1: Overexpressed ,CDK4: Overexpressed	PTEN: Mutation - p.Arg108Gln,PIK3CA: Mutation - P.Glu542Lys	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,RAF: Overexpressed ,JAK1: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,MET: Mutation (SNP) - p.Asp583Asn,KMT2D: Mutation (SNP) - p.Pro876Leu,CDKN2A: Mutation (SNP) - p.Ala89Ser,P53: Stop Gained - p.Ser22*,ALK: Stop Gained - p.Gly1616*

											- CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,FGFR2: Overexpressed ,FGFR1: Overexpressed ,AKT: Overexpressed
Osteosarcoma	Right Distal Tibia	154	No	Dasatinib, Rapamycin	yes	1	21	MEK1: Overexpressed ,CDK4: Overexpressed			RRM1/2: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,FGFR2: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,MET: Mutation (SNP) - p.Gly937Ser,P53: Mutation - p.Trp54*,PDGFRα: Mutation - p.Arg696His,PARP1: Mutation (SNP) - p.Ala451Glu,KMT2D: Mutation - p.Gly3926Arg,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,ALK: Mutation - p.Asn1536Ser
Osteosarcoma	FL distal Radius	196	No	Lapatinib, Trametinib	unknown	0	119	PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,ERBB2 (HER2/neu): Overexpressed			VEGF: Overexpressed ,STAT1: Overexpressed ,JAK1: Overexpressed - CST,FGFR2: Overexpressed ,FGFR1: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,CDKN2A: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	

Osteosarcoma	left humerus	157	No	Rapamycin, Dasatinib, Vorinostat, Imatinib	no	0	126	PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,CDK4: Overexpressed	SETD2: Mutation - p.Lys2184fs	VEGF: Overexpressed ,RRM2: Overexpressed ,MDM2: Overexpressed ,FGFR2: Overexpressed ,FGFR1: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn,NTRK3: Mutation (SNP) - p.Ser42Asn,KMT2C: Mutation (SNP) - p.His906Tyr,ERBB2: Mutation (SNP) - p.Val1189Ile,CDKN2A: Mutation (SNP) - p.Ala89Ser
Osteosarcoma	Left Mandible	153	No	Vorinostat, Rapamycin, Dasatinib	no	0	110				NTRK3: Mutation (SNP) - p.Ser42Asn
Osteosarcoma	Left Distal Radius	143	Yes		yes	1	101				
Osteosarcoma	Left frontal and temporal	109	No	Dasatinib	no	0	36				
Osteosarcoma	LEFT MAXILLARY	130	No	Trametinib, Dasatinib, Rapamycin	unknown	0	98	PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		PIK3CA: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	PDGFRβ: Mutation (SNP) - p.Arg705Cys,NTRK1: Mutation (SNP) - p.Arg220Gln,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,PIK3CA: Mutation - p.Asp454Gly
Osteosarcoma	Thoracic Spine		No		yes	1		PDGFR: Overexpressed ,MYC: Overexpressed ,MEK2: Overexpressed ,CDK4: Overexpressed	PTEN: Mutation - p.Arg313*	TOP2A: Overexpressed ,HIF1a: Overexpressed ,E2F1: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	NTRK1: Mutation (SNP) - p.Arg220Gln,MET: Mutation (SNP) - p.Asp583Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser,BRAF: Mutation (SNP) - p.Ile322Val,EGFR: Mutation - p.Val263Met,BRCA2: Mutation - p.Lys1435Arg
Osteosarcoma	forelimb, distal radius	178	No	Dasatinib, Rapamycin	unknown	0	177				
Osteosarcoma	Left proximal humerus, lungs	74	No	Dasatinib, Rapamycin	yes	1	40				

Osteosarcoma	left thoracic limb		No		no	0					
Osteosarcoma		5	No		no	0					

Table 19: Treatment of Melanoma

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Melanoma	liver	419	No		yes	1		mTOR: Overexpressed - CST,MET: Overexpressed ,ERBB2 (HER2/neu): Overexpressed ,CDK4: Overexpressed	SETD2: Mutation - p.Pro5Gln	ERCC1/2: Underexpressed ,TOP2A: Overexpressed ,RRM1/2: Overexpressed ,PGP: Overexpressed ,MDM2: Overexpressed ,CCND1: Overexpressed ,BCL2: Overexpressed ,AKT: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn,KMT2D: Mutation - p.Gln746Arg,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CDK4: Mutation - p.Cys78Ser	2 Actionable Findings: CDK4, SETD2 3 Additional Findings of Importance: KMT2C, KMT2D, MET	4 Actionable Findings: CDK4, ERBB2, MET, mTOR 8 Additional Findings of Importance: AKT, BCL2, CCND1, MDM2, PGP, RRM1/2, TOP2A, ERCC1/2	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg every other day PO 2. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 3. Lapatinib (ERBB2 inhibitor) - 5-10 mg/kg/day PO 4. Crizotinib (MET inhibitor) - 1-2 mg/kg/day PO 5. Potential tumor resistance to gemcitabine and/or alkylating agents 6. Potential resistance to doxorubicin that may be re-sensitized with Rapamycin 7. Platinum-drug resistance biomarker is expressed in this tumor (MDM2)	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Commonly altered gene family in human malignancies (KMT) 4. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Melanoma	Left maxilla	39	Yes		yes	1									
Melanoma	right cranial thigh region	338	No	Trametinib, Rapamycin	yes	1		MYC: Overexpressed ,MEK1/2: Overexpressed - CST, CDK4: Overexpressed		RRM1/2: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,DHFR: Overexpressed ,COX2: Overexpressed ,CDKN2A: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Arg1237Gln,NOTCH1: Mutation (SNP) - p.Thr14Lys,NTRK3: Mutation (SNP) - p.Ser42Asn,ATM: Mutation - p.Arg2618Lys,P53: Mutation - p.Leu182Pro,KMT2D: Mutation - p.Ser4941Pro,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,ARID1A: Inframe Deletion - p.Gln458del	8 Additional Findings of Importance: ARID1A, KMT2C, KMT2D, P53, ATM, NTRK3, NOTCH1, ROS1	3 Actionable Findings: CDK4, MEK1/2, MYC 16 Additional Findings of Importance: AKT, BCL-XL, CDKN2A, COX2, DHFR, GLUT1, HIF1a, JAK1, JAK2, MDM2, TOP2A, VEGF, BRCA1/2, ERCC1/2, MGMT, RRM1/2	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor resistance to doxorubicin that may be re-sensitized with Rapamycin 7. Potential tumor sensitivity to methotrexate and/or alkylating agents	1. Member of the SWI/SNF family (ARID1A) 2. Commonly altered gene family in human malignancies (KMT) 3. Mutation of well described tumor suppressor gene (P53) 4. Previously identified canine single nucleotide polymorphism (SNP)
Melanoma	pharynx	111	No		yes	1			PTEN: Mutation - p.Asp214fs,		VEGFB: Mutation (SNP) - p.Thr195Ala,VEG				

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
									N-RAS: Mutation - p.Gln61Arg		Fβ: Mutation (SNP) - p.Leu146Val,RO S1: Mutation (SNP) - p.Arg1606His,NO TCH1: Mutation (SNP) - p.Ser1456Asn,M ET: Mutation (SNP) - p.Gly937Ser,FLT 3: Mutation (SNP) - p.Thr142Ile				
Melanoma	right tonsil	5	No		yes	1									
Melanoma	Maxillary mucosa, Palatine tonsil, LN	130	No	Toceranib, Trametinib, Rapamycin, Dasatinib	no	0	12 4	MET: Overexpressed ,MEK1: : Overexpressed ,JAK1: Overexpressed - CST,CDK4: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TYMS: Overexpressed ,NR3C1: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,R OS1: Mutation (SNP) - p.Lys2Arg,NOTC H1: Mutation (SNP) - p.Ser1456Asn,NT RK3: Mutation (SNP) - p.Ser42Asn,MET: Mutation (SNP) - p.Asp583Asn,KM T2D: Mutation - p.Ala3629Thr,KM T2C: Inframe Insertion - p.Lys3163_Leu31 64insAsnLys,CR EBBP: Mutation - p.Thr1923Ile,BR	9 Additional Findings of Importance : BRCA2, CREBBP, KMT2C, KMT2D, MET, NTRK3, NOTCH1, ROS1(2)	4 Actionable Findings: CDK4, JAK1, MEK1, MET 8 Additional Findings of Importance: HIF1a, MDM2, NR3C1, TYMS, BRCA1/2, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Crizotinib (MET inhibitor) - 1-2 mg/kg/day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Apoquel (JAK1 inhibitor) - dose per label 5. Potential therapeutic benefit of glucocorticoids. 6. Potential tumor sensitivity to 5-FU, alkylating agents and/or platin based chemotherapy.	1. Tumor suppressor gene (BRCA2) 2. Feature of malignant transformation (CREBBP) 3. Commonly altered gene family in human malignancies (KMT) 4. Canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											CA2: Mutation (SNP) - p.Pro2221Leu			7. Potential tumor resistance to doxorubicin.	
Melanoma	Left Caudal palatogloss al arch	329	No	Trametinib, Rapamycin	yes	1	183	MYC: Overexpressed ,MET: Overexpressed ,MEK1/2: Overexpressed - CST,CDK4: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,HIF1a: Overexpressed ,DHFR: Overexpressed ,CDKN2A: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	P53: Mutation - p.Pro291_Gly292fs,MET: Mutation (SNP) - p.Asp583Asn,KMT2D: Mutation - p.Gln746Arg,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Gln2231_Gln2232insGlnGln,BRCA1: Mutation - p.Thr1864Ile	6 Additional Findings of Importance: BRCA1, CREBBP, KMT2C, KMT2D, MET, P53	5 Actionable Findings: CDK4, MEK1/2, MET, MYC 12 Additional Findings of Importance: AKT, CCND1, CDKN2A, DHFR, HIFa, JAK1, RAS/RAF, STAT1, VEGF, BRCA1/2, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Crizotinib (MET inhibitor) - 1-2 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor sensitivity to alkylating and/or platin based chemotherapy.	1. Tumor supressor gene (BRCA1) 2. Feature of malignant transformation (CREBBP) 3. Commonly altered gene family in human malignancies (KMT) 4. Mutation of well described tumor suppressor gene P53. 5. Previously identified canine single nucleotide polymorphism (SNP)
Melanoma	Right metacarpal paw pad	126	No	Trametinib, Rapamycin, Dasatinib	no	0	114	MYC: Overexpressed ,MEK1/2: Overexpressed -		RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2:		DNA failed sequencing	3 Actionable Findings: CDK4, MEK1/2, MYC 8 Additional Findings of Importance:	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Vorinostat	DNA failed sequencing

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Underexpressed ,TYMS: Overexpressed ,CDKN2A: Overexpressed ,AKT: Overexpressed			AKT, CDKN2A, TYMS, BRCA1/2, ERCC1/2, MGMT, PGP, RRM1/2	(HDAC inhibitor) - 30 mg/kg/every other day PO 4. Potential tumor sensitivity to 5'FU, gemcitabine, alkylating agents and/or platin based agents	
Melanoma	Left front 3rd digit	423	No	Trametinib, Apoquel, Dasatinib	yes	1	120	MYC: Overexpressed ,MEK1/2: Overexpressed - CST,CDK4: Overexpressed		STAT1: Overexpressed ,RRM2: Overexpressed ,RAS/RAF: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,GLUT1: Overexpressed ,CDKN2A: Overexpressed ,AKT: Overexpressed		Unfortunately, DNA sequencing failed for the given sample.	4 Actionable Findings: CDK4, JAK1, MEK1/2, MYC 7 Additional Findings of Importance: AKT, CDKN2A, GLUT1, JAK2, RAS/RAF, RRM2, STAT1	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Oclacitinib (JAK inhibitor) - dose per label 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Potential tumor resistance to gemcitabine.	Unfortunately, DNA sequencing failed for the given sample.
Melanoma	lip with metastasis to mandibular LN	212	Yes		yes	1		MET: Overexpressed ,CDK4: : Overexpressed	N-RAS: Mutation - p.Gln61Arg	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,PTEN:	ROS1: Mutation (SNP) - p.Thr2260Met,P53: Mutation - p.Arg201*,P53: Mutation - p.Ile241Phe,KMT2D: Mutation - p.Ala4269Val,KMT2C: Inframe Insertion -	1 Actionable Findings: N-RAS 6 Additional Findings of Importance: BRCA2,	2 Actionable Findings: CDK4, MET 8 Additional Findings of Importance: BCL2, JAK1, PTEN, BRCA1/2, ERCC1/2,	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Crizotinib (MET inhibitor) - 1-2 mg/kg/day PO 3. Potential tumor sensitivity to gemcitabine, alkylating agents	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Tumor suppressor gene (BRCA2) 3. Commonly

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed ,JAK1: Overexpressed - CST,BCL2: Overexpressed	p.Lys3163_Leu3164insAsnLys,BRCA2: Mutation (SNP) - p.Asn2929Asp	KMT2C, KMT2D, P53(2), ROS1	MGMT, PGP, RRM1/2	and/or platin based agents	altered gene family in human malignancies (KMT) 4. Mutation of well described tumor suppressor gene (P53) 5. Previously identified canine single nucleotide polymorphism (SNP)
Melanoma	metastatic lymph node	364	No	Toceranib, Crizotinib	yes	1	122								
Melanoma	Oral submucosa	209	Yes	Dasatinib, Deramaxx, Rapamycin, Toceranib	yes	1	152		SETD2: Mutation - p.Gln2129Arg		ROS1: Mutation (SNP) - p.Thr2260Met,CREBBP: Mutation - p.Pro2046_Gln2047del,ABL1: Mutation - p.Gly807Ser,BRCA2: Mutation - p.Met3332_Lys3333insIleLys				
Melanoma	Rostral Mandible	200	No		no	0		CDK4: Overexpressed		MDM2: Overexpressed ,AKT: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn,KMT2C: Mutation - p.3163_3164insA	3 Additional Findings of Importance:	1 Actionable Finding: CDK4 2 Additional	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Potential tumor	1. Mutation of well described tumor suppressor

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											snLys,BRCA2: Mutation - p.Met3332Lys	BRCA2, KMT2C, MET	Findings of Importance: AKT, MDM2	resistance to doxorubicin.	gene (BRCA2). 2. Commonly altered gene family in human malignancies . 3. Previously identified canine single nucleotide polymorphism (SNP).
Melanoma	R Forelimb Prescapular Area	278	No	Rapamycin, Trametinib	yes	1	89	MYC: Overexpressed ,MET: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST	K-RAS: Mutation - p.Gly12Cys, EGFR: Mutation - p.Gly466Ala	VEGF: Overexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,PDGF: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed ,BCL2: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,ROS1: Mutation (SNP) - p.Ile133Val,KMT2D: Mutation - p.Gln3811del	2 Actionable Findings: EGFR, K-RAS 3 Additional Findings of Importance: KMT2D, ROS1(2)	4 Actionable Findings: JAK1, MEK1/2, MET, MYC 11 Additional Findings of Importance: AKT, BCL2, COX2, GLUT1, HIF1a, JAK2, MDM2, PDGF, RAS/RAF, STAT1, VEGF	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Apoquel (JAK inhibitor) - dose per label 3. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Potential therapeutic benefit of NSAIDs. 6. Potential tumor sensitivity to platinum based agents. 7. Biomarkers associated with radiotherapy and chemotherapy	1. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Commonly altered gene family in human malignancies (KMT). 4. Canine single nucleotide polymorphisms (SNPs).

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														resistance. 8. Intracellular signaling via MAPK/ERK and/or AKT/PI3K/mTOR pathways.	
Melanoma	oral	1022	No	Dasatinib, Rapamycin	yes	1	84	MYC: Overexpressed ,MET: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	MET: Mutation - p.Ala404Val	STAT1: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,CDKN2A: Overexpressed ,AKT: Overexpressed	PDGFRβ: Mutation (SNP) - p.Arg705Cys,NF1: Mutation - p.Ser1747*,MET: Mutation (SNP) - p.Asp583Asn,FLT3: Mutation (SNP) - p.Thr142Ile,BRCA2: Mutation (SNP) - p.Asn2929Asp,ARID1A: Mutation - p.Ala822Thr	1 Actionable Finding: MET 6 Additional Findings of Importance: ARID1A, BRCA2, FLT3, MET, NF1, PDGFRβ	5 Actionable Findings: CDK4, JAK1, MEK1/2, MET, MYC 6 Additional Findings of Importance: AKT, CDKN2A, HIF1a, MDM2, RAS/RAF, STAT1	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Apoquel (JAK inhibitor) - dose per label 6. Potential tumor resistance to doxorubicin which may be resensitized with Rapamycin. 7. Biomarkers associated with generalized chemo and radiation resistance.	1. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 2. Mutated gene often identified in human melanoma (NF1). 3. Mutation of tumor suppressor gene (BRCA2). 4. Canine single nucleotide polymorphisms (SNPs).
Melanoma	Lower left Jaw	239	No	Rapamycin, Dasatinib,	yes	1	33	MYC: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed	RB1: Mutation - p.Cys712fs,P53: Mutation - p.Val264Asp,NO	4 Additional Findings of Importance	5 Actionable Findings: CDK4, JAK1, MEK1/2,	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO	1. Mutation of tumor suppressor gene (RB1).

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Melanoma	Fourth Digit Right	224	No	Rapamycin, Trametinib	yes	1	32	MYC: Overexpressed	K-RAS: Mutation - p.Gly13Asp	PGP: Underexpressed ,MGMT: Underexpressed	NOTCH1: Mutation - p.Glu643Lys,KM T2C: Inframe	1 Actionable Finding: K-RAS	5 Actionable Findings: CDK4, JAK1, MEK1/2,	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO	1. Trametinib (MEK inhibitor) - 0.02
				Trametinib				.MET: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		.ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,CDKN2A: Overexpressed ,BCL2: Overexpressed ,AKT: Overexpressed	TCH1: Mutation (SNP) - p.Ser1456Asn,CREBBP: Mutation - p.Gly59Ser	: CREBBP, NOTCH1, P53, RB1	MET, MYC 13 Additional Findings of Importance: AKT, BCL2, CCND1, CDK2A, HIF1a, JAK2, MDM2, RAS/RAF, VEGF, BRCA1/2, ERCC1/2, MGMT, PGP	2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Apoquel (JAK1 inhibitor) - dose per label 6. Potential tumor sensitivity to alkylating agents (low MGMT) and platinum (low BRCA1/2 and ERCC1/2) chemotherapy agents 7. Biomarkers associated with generalized radiation and chemotherapy resistance. 8. Potential intracellular signaling including JAK/STAT and RAS/RAF/MEK pathways.	2. Mutation of well described tumor suppressor gene (P53). 3. Feature of malignant transformation (CREBBP). 4. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
	Forepaw, lungs, right shoulder							,MET: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,STAT1: Overexpressed ,RRM2: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	Insertion - p.Lys3163_Leu3164insAsnLys,ERBB2: Mutation (SNP) - p.Ala191Thr	3 Additional Findings of Importance: ERBB2, KMT2C, NOTCH1	MET, MYC 12 Additional Findings of Importance: AKT, CCND1, HIF1a, JAK2, MDM2, RAS/RAF, RRM2, STAT1, BRCA1/2, ERCC1/2, MGMT, PGP	2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 5. Apoquel (JAK1 inhibitor) - dose per label 6. Biomarkers associated with generalized chemoresistance. 7. Potential tumor sensitivity to platinum based agents.	mg/kg/day PO 2. Commonly altered gene family in human malignancies (KMT). 3. Canine single nucleotide polymorphisms (SNPs).
Melanoma	left submandibular lymph node (metastasis from oral melanoma originally removed	487	No	Rapamycin, Trametinib, Dasatinib, Vorinostat	yes	1	116	MET: Overexpressed ,MEK1/2: Overexpressed - CST,CDK4: Overexpressed	SETD2: Mutation - p.Tyr1268Phe	TOP2A: Overexpressed ,RRM1/2: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,CDKN2A: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	NOTCH1: Mutation (SNP) - p.Ser1456Asn,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	1 Actionable Findings: SETD2 2 Additional Finding of Importance: KMT2C, NOTCH1	3 Actionable Findings: CDK4, MEK1/2, MET 7 Additional Findings of Importance: AKT, CCND1, CDKN2A, HIF1a, MDM2, RRM1/2, TOP2A	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Dasatinib (CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 4. Biomarkers associated with generalized chemo and radiation resistance. 5. Potential tumor	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Commonly altered gene family in human malignancies (KMT). 3. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
	from lip)													resistance to gemcitabine.	
Melanoma	Oral	335	Yes	Dasatinib, Rapamycin, Toceranib, Imatinib	yes	1	115								
Melanoma	left hind digit 3 (not 4)	294	No		yes	1		MEK1/2: Overexpressed - CST,CDK4: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,STAT1: Overexpressed ,RRM2: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,CCND1: Overexpressed	PDGFRβ: Mutation (SNP) - p.Arg705Cys,FLT3: Mutation - p.Val186Leu,ABL1: Mutation (SNP) - p.Ala925Thr,P53: Mutation - p.Arg327Cys,CDKN2A: Mutation - p.Pro24fs	5 Additional Findings of Importance: CDKN2A, P53, ABL1, FLT2, PDGFRB	2 Actionable Findings: CDK4, MEK1/2 12 Additional Findings of Importance: CCND1, HIF1a, JAK1, MDM2, RAS/RAF, RRM2, STAT1, TOP2A, BRCA1/2, ERCC1/2, MGMT, PGP	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor resistance to doxorubicin that may be re-sensitized with Rapamycin. 5. Potential tumor resistance to gemcitabine 6. Potential tumor sensitivity to alkylating agents	1. Cyclin-dependent kinase inhibitor 2A (CDKN2A) 2. Mutation of well described tumor suppressor gene (P53) 3. Previously identified canine single nucleotide polymorphism (SNP)
Melanoma	Oral Cavity	88	Yes	Rapamycin, Trametinib, Vorinostat	yes	1	118				ROS1: Mutation (SNP) - p.Thr2260Met,NOTCH1: Mutation (SNP) - p.Ser1456Asn,CDKN2A: Mutation	10 Additional Findings: ABL1, FLT1, KMT2C, BRCA1(4),			1. Cell migration and adhesion gene control (ABL1) 2. Tumor

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											(SNP) - p.Ala89Ser,BRCA1: Mutation (SNP) - p.Lys155Glu,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation (SNP) - p.Arg337Ser,BRCA1: Mutation (SNP) - p.Ala1873Thr,KMT2D: Mutation - p.Asp1549frameshift,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FLT1: Mutation - p.Lys486Arg,ABL1: Mutation - p.Gly665Arg	CDKN2A, NOTCH1, ROS1			angiogenesis and cell survival surface receptor (FLT1) 3. Commonly altered gene family in human malignancies (KMT) 4. Previously identified canine single nucleotide polymorphism (SNP).
Melanoma	Oral Cavity	153	No	Imatinib, Toceranib	no	0	77		JAK1: Mutation - p.Arg826Cys ,PDGFRα: Mutation - p.Arg558Cys		ROS1: Mutation (SNP) - p.Thr2260Met,FLT3: Mutation (SNP) - p.Thr142Ile,BRCA1: Mutation (SNP) - p.Lys155Glu,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation	11 Additional Findings of Importance : ABL1, BRCA2, JAK1, PDGFRα, RET, BRCA1(4), FLT3, ROS1		1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Crizotinib (MET	1. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 2. Toceranib (PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Oclacitinib

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											(SNP) - p.Arg337Ser,BRCA1: Mutation (SNP) - p.Ala1873Thr,RET: Inframe Insertion - p.Thr7_Ala8insThrAlaThr,BRCA2: Mutation (SNP) - p.Asn2929Asp,ABL1: Mutation - p.Gly665Arg			inhibitor) - 1-2 mg/kg/day PO	(JAK inhibitor) - dose per label 4. Control cell migration and adhesion (ABL1) 5. Tumor suppressor gene (BRCA2) - potential benefit from DNA damaging agents 4. Tyrosine kinase receptor (RET) 5. Previously identified canine single nucleotide polymorphism (SNP)
Melanoma	right upper lip	378	No	Rapamycin, Dasatinib, Trametinib	yes	1	1 2 4		NF1: Mutation - p.Glu1347*,MET: Mutation - p.Ile233Asn,PDGFRβ: Inframe Insertion - p.Ala1064_Asp1065insAlaAsnLeu,ALK: Mutation - p.Ala1200Val,KIT: Mutation - p.Asp816Val		ROS1: Mutation (SNP) - p.Ile133Val,MET: Mutation (SNP) - p.Asp583Asn,KIT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,BRCA2: Mutation -			

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
									p1065insAlaAsp		p.Met3332_Lys3333insIleLys,BRCA1: Mutation (SNP) - p.Ala1873Thr,BRCA1: Mutation - p.Thr1101Ala				
Melanoma	Lip and lymph node	401	Yes	Rapamycin, Dasatinib	yes	1	32	MYC: Overexpressed ,MET: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		STAT1: Overexpressed ,RAS/RAF: Overexpressed ,NR4A2: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,PDGFRβ: Mutation (SNP) - p.Arg705Cys,JAK2: Mutation (SNP) - p.Ile19Val,KMT2C: Mutation - p.3163_3164insAsnLys,BRCA2: Mutation (SNP) - p.Asn2929Asp	5 Additional Findings of Importance: BRCA2, KMT2C, JAK2, PDGFRβ, ROS1	6 Actionable Findings: CDK4, JAK1, MEK1/2, MET, MYC 6 Additional Findings of Importance: AKT, HIF1a, MDM2, NR4A2, RAS/RAF, STAT1	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 4. Apoquel (JAK inhibitor) - dose per label 5. Vorinostat (HDAC inhibitor) - 45 mg/kg/every other day PO 6. Biomarkers associated with generalized chemoresistance. 7. Potential intracellular signaling via JAK/STAT and/or MAPK/ERK pathways.	1. Mutation of well described tumor suppressor gene (BRCA2). 2. Commonly altered gene family in human malignancies . 3. Canine single nucleotide polymorphisms (SNPs).
Melanoma	Dorsal/Caudal	175	Yes	Dasatinib, Rapamycin	yes	1	47	MET: Overexpress	ATM: Mutation -	RAS/RAF: Overexpressed ,MDM2:	NOTCH1: Mutation - p.Pro1003Leu,P5	1 Actionable Finding:	3 Actionable Findings: CDK4,	1. Dasatinib (Src inhibitor) - 0.5-0.7 mg/kg/every other	1. Vorinostat (HDAC inhibitor) - 45

Tumor type	Tumor Location	Total Survival time (days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significance Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
	Tongue							ed ,MEK2 : . Overexpressed ,CDK4 : . Overexpressed	p.Ser1361Arg	Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,COX2: Overexpressed ,AKT: Overexpressed	3: Mutation - p.Trp80*	ATM 2 Additional Findings of Importance : P53, NOTCH1	MEK2, MET 6 Additional Findings of Importance: AKT, COX2, CCND1, HIF1a, MDM2, RAS/RAF	day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 4. Potential therapeutic benefit of NSAIDs. 5. Potential tumor resistance to doxorubicin. 6. Biomarkers associated with generalized chemo and radiation resistance as well as a highly proliferative phenotype.	mg/kg/every other day PO 2. Mutation of well described tumor suppressor gene (P53). 3. Canine single nucleotide polymorphism (SNP)(NOTCH1).
Melanoma	Right caudal maxilla	178	No	Rapamycin, Dasatinib	no	0	159	MET: Overexpressed ,MEK2 : . Overexpressed ,CDK4 : . Overexpressed	SETD2: Mutation - Gly594Asp	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed	JAK2: Mutation (SNP) - p.Ile19Val,KMT2C: Mutation (SNP) - p.His906Tyr	1 Actionable Finding: SETD2 2 Additional Findings of Importance : KMT2C, JAK2	3 Actionable Findings: CDK4, MEK2, MET 9 Additional Findings of Importance: CDKN2A, GLUT1, HIF1a, MDM2, TOP2A, VEGF, ERCC1/2, MGMT, PGP,	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 4. Biomarkers associated with generalized chemo and radiation resistance. 5. Potential	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Mutated gene family commonly seen in human malignancies (KMT2C). 3. Canine single nucleotide

Tumor type		
Tumor Location		
Total Survival time (days)		
Radiation		
Targeted Drugs		
Previous cancer therapy		
Traditional Therapy Refractory (yes=1, no =0)		
Total Days on Targeted Drugs		
Actionable RNA Alterations		
Potentially Clinically Significant Findings		
Other RNA Alterations	,CDKN2A: Overexpressed	
Other Potentially Clinical Significance Findings		
DNA Sequencing Findings		
Gene Expression Findings		
RNA Therapeutic Indications	sensitivity to anthracyclines, platin based and alkylating agents. 6. Expression profile associated with poor prognosis in humans.	
DNA Therapeutic Indications	polymorphism (SNP)	

Table 20: Treatment of Mast Cell Tumors

Tumor type	Tumor Location	Total Survival time (in days)	Radiation	Targeted Drugs	Previous cancer	Traditional Therapy Refractory (yes=1)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Mast Cell Tumor	Left hip extending to perineum	225	No	Imatinib	yes	1	11				
Mast Cell Tumor	multi focal	151	No	Imatinib	yes	1	18				
Mast Cell Tumor		342	No	Imatinib	yes	1	22				
Mast Cell Tumor		297	No	Imatinib	yes	1	16	1 Actionable Findings: SETD2 3 Additional Finding of Importance: BRCA1, CDK2A, ROS1	6 Actionable Findings: CDK4, KDR, KIT, JAK1, MEK1/2, MYC 11 Additional Findings of Importance: AKT, BCL6, CCND1, ERCC2, JAK2, MDM2, RRM2, VEGF, BRCA1/2, MGMT, PGP	1. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Apoquel (JAK inhibitor) - dose per label 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Potential tumor sensitivity to alkylating chemotherapy agents	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Mutation of well described tumor suppressor gene (BRCA2). 3. Canine single nucleotide polymorphism (SNP).
Mast Cell Tumor	High-grade 2	397	Yes		yes	1		Unfortunately, the tissue biopsy failed DNA library prep. No DNA results available.	4 Actionable Findings: CDK4, KIT, JAK1, KDR, MEK1/2 11 Additional Findings of Importance: AKT, CCND1, HIF1a, JAK2, RAS/RAF, RRM2, VEGF, BRCA1/2, ERCC1/2, MGMT, PGP	1. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Apoquel (JAK inhibitor) - dose per label 5. Generalized biomarkers of chemo and radiation resistance. 6. Potential tumor sensitivity to alkylating and platin based chemotherapy agents.	Unfortunately, the tissue biopsy failed DNA library prep. No DNA results available.
Mast Cell Tumor	Left prescap area	43	No	Sorafenib	yes	1	14				

Mast Cell Tumor	Liver, intestines	111	No	Trametinib	yes	1	1	4 Additional Findings of Importance: CREBBP, MIEN1, P53, ABL1	2 Actionable Findings: JAK1, MEK1/2 17 Additional Findings of Importance: AKT, BCL6, COX2, CDKN2A, DHFR, HIF1a, JAK2, MDM2, PGP, PTEN, RAS/RAF, STAT1, RRM2, TYMS, VEGF, BRCA1/2, ERCC1/2	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Apoquel (JAK inhibitor) - dose per label 3. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 4. Potential tumor resistance to gemcitabine, vinca alkaloids and/or alkylating agents. 5. Potential tumor sensitivity to 5FU. 6. Platinum-drug resistance biomarker is expressed in this tumor (MDM2)	1. Feature of malignant transformation (CREBBP) 2. Small membrane bound protein (MIEN1) 3. Mutation of well described tumor suppressor gene P53. 4. Previously identified canine single nucleotide polymorphism (SNP)
Mast Cell Tumor	Right Rostral Maxilla	5	No		unknown	0					1. Toceranib (KIT/KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KIT inhibitor) - 10 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO	
Mast Cell Tumor	Nasal planum with metastasis to left submandibular lymph node	882	Yes		yes	1						
Mast Cell Tumor	L lateral thigh 2x4cm derm/SQ, high-grade, MI 11/10hpf (5mm micro margins) -- clean excision L lateral thigh 1cm derm, low-grade, MI 3/10hpf (2-3mm micro margins) -- clean excision 9/3/19 L lateral thigh ~8mm derm, high-grade, MI 20/10hpf (12.6mm micro margins) - - clean excision L inguinal subcutaneous mass, Feb 2020: metastatic MCT to LN	244	No		yes	1		1 Mutations Identified: ROS1			UNKOWN CLINICAL SIGNIFICANCE ROS1: Previous identified as a SNP in canine.	
Mast Cell Tumor	Right cranial thigh	75	Yes	Toceranib	yes	1	16					
Mast Cell Tumor	Left prescapular lymph node	349	Yes	Dasatinib	yes	1	9					

Mast Cell Tumor	Dorsal thorax	263	No	Trametinib, Vorinostat	yes	1	28					
Mast Cell Tumor	R. Neck	518	No	Toceranib, Imatinib	unknown	0	262					
Mast Cell Tumor	Lip, Right and left medial elbows, neck	162	Yes	Imatinib, Vorinostat, Chlorambucil, Sorafenib	yes	1	309					
Mast Cell Tumor	Right side of face, extending into neck	237	No	Imatinib	yes	1	22					
Mast Cell Tumor	L popliteal lymph node	325	No	Imatinib	yes	1	25					
Mast Cell Tumor	Limb - but not sure	295	No	Toceranib, Imatinib, Sorafenib	no	0	24					
Mast Cell Tumor	left ear base	132	No	Toceranib	no	0	115					
Mast Cell Tumor	-left side of face (1cm) - right medial thigh (0.5cm) -4 preputial and periopreputial (two cranial to prepuce, one right and one left of midline, two on prepuce, one on left and one on right) (range 0.5-1cm) -left ischial region (previous scar) (largest mass, ~1.5cm) -2 perianal masses (one right (1cm), two left (0.5cm)) -left perineal mass (0.5cm) - two masses at right caudomedial thigh (0.5cm each) 12 total masses removed	1028	Yes	Imatinib, Trametinib	yes	1	218					
Mast Cell Tumor	Right Flank	80	No	Imatinib, Sorafenib, Rapamycin	yes	1	20					
Mast Cell Tumor	Left Shoulder, Right Flank and tail base	468	No	Toceranib, Imatinib, Rapamycin	yes	1	140	1 Actionable Findings: mTOR 4 Additional Findings of Importance: ARID1A, BRAF, MET, ROS1	6 Actionable Findings: CDK4, JAK1, KDR, KIT, MEK1/2, PDGFR 9 Additional Findings of Importance: AKT, BCL-XL, CCND1, HIF1a, JAK2, STAT1,	1. Imatinib (KIT/KDR/PDGFR inhibitor) - 10 mg/kg/day PO 2. Palladia (KIT/KDR/PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK1/2 inhibitor) - 0.02 mg/kg/day PO 5. Apoquel (JAK inhibitor) - dose per label	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Canine single nucleotide polymorphisms (SNPs).

Mast Cell Tumor	cytology only	172	No	Toceranib, Imatinib	no	0	140					
Mast Cell Tumor	SQ Mass - Ventral Chest	454	No	Toceranib, Imatinib	no	0	35					
Mast Cell Tumor	Skin/subcutis, dorsal caudal neck	245	No	Toceranib, Imatinib	yes	1	184	Unfortunately, DNA extraction for this sample failed.	4 Actionable Findings: CDK4, KIT, KDR, MEK1/2 12 Additional Findings of Importance: AKT, BCL2, BCL6, BCL-XL, CCND1, E2F1, ERCC1/2, MGMT, RAS/RAF, RRM1/2, TOP2A, VEGF	1. Toceranib (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 5. Potential tumor resistance to gemcitabine, alkylating agents and/or platin based agents 6. Potential tumor sensitivity to doxorubicin	DNA results are not available.
Mast Cell Tumor	Cutaneous	324	No	Toceranib, Imatinib	no	0	81					
Mast Cell Tumor	left prescapular area	296	No	Toceranib, Imatinib	yes	1	136					
Mast Cell Tumor	Right prescapular region	340	No	Vorinostat	yes	1	14	2 Actionable Findings: NOTCH1, SETD2 7 Additional Findings: ARID1A, CREBBP(2), FGFR3, SMARCA4(2), CDKM2A	4 Actionable Findings: CDK4, KDR, MEK1/2, MYC 10 Additional Findings of Importance: HIF1a, JAK1, JAK2, RAF, RRM2, STAT1, TYMS, BRCA1/2, ERCC1/2, MGMT	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 5. Potential tumor resistance to gemcitabine 6. Potential tumor sensitivity to methotrexate, 5'FU, platin agents and/or alkylating agents	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Member of the SWI/SNF family (ARID1A) 3. Feature of malignant transformation (CREBBP) 4. Polypeptide growth factor gene (FGFR3) 5. Component of SWI/SNF protein complexes (SMARCA4) 6. Previously identified canine single nucleotide

													polymorphism (SNP).	
	Mast Cell Tumor	medial aspect of left elbow	199	No	Toceranib, Imatinib	no	0	143						
	Mast Cell Tumor	Left flank and inguinal region	106	No			0		3 Actionable Findings: KIT, SETD2(2) 21 Additional Findings of Importance: ALK(3) ARID1A, ATRX(2), BRCA2, FGFR2IIIC(2), KMT2C(2), P53(3), PDGFRA, PTPRD, NOTCH1, ROS1(2), VEGFB(2)		1. Toceranib (KIT/KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KIT inhibitor) - 10 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO	1. Toceranib (KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KIT inhibitor) - 10 mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Tyrosine kinase receptors (ALK, PDGFR) 5. Member of the SWI/SNF family (ARID1A) 6. Tumor supressor gene (ATRX) 7. Potential sensitivity to platin based agents (BRCA2) 8. Fibroblast growth factor receptor (FGFR2IIIC) 9. Commonly altered gene family in human malignancies (KMT) 10. Potential resistance to anthracyclines, alkylating, antimetabolites and platin based agents (P53) 11. Protein tyrosine phosphatase family (PTPRD) 12. Canine single nucleotide polymorphism (SNP).

Mast Cell Tumor	Left hind leg	289	Yes	Imatinib	yes	1	28	6 Additional Findings: CDK4, RET, CDKN2A, KMT2C, KMT2D, MET			1. Cyclin dependent kinase protein that regulates cell cycle (CDK4) 2. Tyrosine kinase receptor (RET) 3. Canine single nucleotide polymorphism (SNP).
Mast Cell Tumor		27		Imatinib	unknown	0	27				

Table 21: Treatment of Mammary Carcinoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Mammary Carcinoma	left mammary chain, left prescapular/axillary /inguinal lymph nodes, skin nodules	327	No		yes	1				ROS1: Mutation (SNP) - p.Arg1606His,PDGFRα: Mutation - p.Arg696His,KMT2C: Stop Gained - p.Arg1395*,FBXW7: Mutation - p.Arg470His,FBXW7: Stop Gained - p.Arg14*,BRCA2: Mutation - p.Met3332Lys,BRCA2: Mutation - p.Asn636_Cys637fs,PDGFRβ: Mutation - p.Glu400Lys	8 Additional Findings of Importance: BRCA2(2), FBXW7(2), KMT2C, PDGFRα, PDGFRβ, ROS1		1. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO	1. Tumor suppressor genes (BRCA2, FBXW7) 2. Commonly altered gene family in human malignancies (KMT) 3. Gene involved in cell proliferation (PDGFR) 4. Previously identified canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Mammary Carcinoma	mammary gland	240	No		no	0		K-RAS: Mutation - p. Gly106Asp		ROS1: Mutation (SNP) - p.Thr2260Met,ROS1: Mutation (SNP) - p.Ile133Val,BRAF: Mutation (SNP) - p.Ile322Val,KMT2C: Mutation - p. Asp1321Tyr,VEGFB: Mutation (SNP) - p.Thr195Ala,CREBBP : Mutation - p. Pro2046_Gln2047del				
Mammary Carcinoma	left m4	107	No	Lapatinib	no	0	0	NOTCH1: Mutation - p. Val2035Leu,P53: Mutation - p. Ala148Asp,SETD 2: Mutation - p.Tyr1268Phe		CREBBP: Inframe Deletion - p. Pro2046_Gln2047del, FLT3: Mutation - p.Thr153Ile,NOTCH1: Mutation (SNP) - p.Ser1456Asn,MET: Mutation (SNP) - p.Asp583Asn,ROS1: Mutation (SNP) - p.Thr2260Met				
Mammary Carcinoma	Left caudal mammary gland (Surgery 2/2019), pulmonary metastasis 5/2020	937	Yes		yes	1		SETD2: Mutation - p.Ala555Pro,RET : Mutation - p.Ala465Gly,NOTCH1: Mutation - p.Thr2278Pro		NOTCH1: Mutation (SNP) - p.Val2035Ile,CREBBP : Mutation - p.Gly59Ser,ATRX: Mutation - p.Glu873Lys,ATRX: Mutation - p.Thr763Ala,ARID1A: Inframe Deletion - p.Gln458del,ABL1: Mutation (SNP) - p.Leu830Phe				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Mammary Carcinoma	Right inguinal mammary gland	43	No		no	0		FBXW7: Stop Gained - p.Gln625*		PDGFRβ: Mutation (SNP) - p.Arg705Cys,ABL1: Mutation (SNP) - p.Leu830Phe				
Mammary Carcinoma	Right 4th and 5th mammary glands	241	No	Imatinib, Rapamycin, Toceranib	yes	1	64		MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed ,RRM1/2: Overexpressed ,RAS/RAF: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,CDKN2A: Overexpressed ,CCND1: Overexpressed ,BCL-XL: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed	P53: Mutation - p.Phe331Ser,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Gly59Ser	3 Additional Findings of Importance: CREBBP, P53, KMT2C	7 Actionable Findings: CDK4, EGFR, ERBB2, KDR, KIT, MEK1/2, MYC 13 Additional Findings of Importance: AKT, BCL6, BCL-XL, CCND1, CDKN2A, GLUT1, HIF1a, RAS/RAF, RRM1/2, TOP2A, VEGF, ERCC1/2, MGMT	1. Lapatinib (ERBB2/EGFR inhibitor) - 5-10 mg/kg/day PO 2. Imatinib (KIT/KDR inhibitor) - 10 mg/kg/day PO 3. Palladia (KIT/KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 6. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 7. High expression of genes involved in	1. Mutation of well described tumor suppressor gene (P53). 2. Commonly altered gene in human malignancies (KMT). 3. Feature of malignant transformation (CREBBP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
													hypoxia and neovascularization impacting in chemoresistance and metastasis 8. Gene profile is favorable to chemotherapy response to doxorubicin, 5-fluoruoacil, and alkylating agents. 9. Tumor signaling via MEK/MAPK and AKT/RAS/RAF intracellular pathways.	
Mammary Carcinoma	Mammary glands	94	No		no	0		FLT3: Mutation - p.Val186Leu,FLT3: Mutation - p.Asp748Asn		VEGFC: Mutation - p.Val342Ile,ROS1: Mutation (SNP) - p.Thr2260Met,KMT2D: Mutation - p.Val4565Ala,KMT2D: Mutation (SNP) - p.Val4565Ala,KMT2C: Mutation (SNP) - p.Pro4236Leu				
Mammary Carcinoma	mammary glands L3-5	132	No	Trametinib, Rapamycin	no	0	96	EGFR: Mutation - p.Pro236Leu,mTOR: Mutation - p.Tyr2072Ser,NOTCH1: Mutation - p.Val2035Ile		MET: Mutation (SNP) - p.Gly937Ser,EGFR: Mutation (SNP) - p.Arg202Gln,RTP2: Mutation (SNP) - p.His97Tyr,KMT2D:				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Mutation - p.Pro895_Arg904del				
Mammary Carcinoma	Right mammary #5	102	No		no	0		PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot) ,K-RAS: Mutation - p.Gly12Val	VEGF: Overexpressed ,TOP2A: Overexpressed ,RRM1/2: Overexpressed ,PTEN: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,COX2: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,ROS1: Mutation (SNP) - p.Arg1606His,ROS1: Mutation (SNP) - p.Ile133Val,MET: Mutation (SNP) - p.Gly937Ser,JAK2: Mutation (SNP) - p.Ile19Val,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation - p.Gly264Asp	2 Actionable Findings: K-RAS, PIK3CA 7 Additional Findings of Importance: BRCA1(2), JAK2, MET, ROS1(3)	4 Actionable Findings: EGFR, MEK1/2, MET, MYC 7 Additional Findings of Importance: COX2, HIF1a, MDM2, PTEN, RRM1/2, TOP2A, VEGF	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 3. Crizotinib (MET inhibitor) - 1-2 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 6. Biomarkers associated with generalized chemo-resistance 7. Potential tumor resistance to gemcitabine 8. Potential	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 3. Tumor supressor gene (BRCA1) 4. Previously identified canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
													tumor resistance to doxorubicin that may be re-sensitized with rapamycin.	
Mammary Carcinoma	Mammary	111	No	Vorinostat	no	0	44	NOTCH1: Inframe Insertion - p.Cys1171_Gly1172insCysGlyTrpAspGlyGly		PTPRD: Mutation - p.Glu552Lys,KMT2D: Mutation - p.Leu990Ser,FGFR2IIIC: Mutation - p.Gly67Val,CREBBP: Mutation - p.Val1060_Glu1061fs, CDK4: Mutation - p.Cys78Ser	1 Actionable Findings: NOTCH1 5 Additional Findings: CDK4, CREBBP, FGFRIIIC, KMT2D, PTPRD			1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Cyclin dependent kinase protein that regulates cell cycle (CDK4) 3. Feature of malignant transformation (CREBBP) 4. Fibroblast growth factor receptor (FGFR) 5. Commonly altered gene family in human malignancies (KMT) 6. Protein tyrosine phosphatase

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														family (PTPRD).
Mammary Carcinoma	Right mammary chain, first gland	657	No	Rapamycin, Dasatinib, Lapatinib, Vorinostat	yes	1	414	NOTCH1: Mutation (SNP) - p.Val2035Ile	MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,BCL2: Overexpressed ,AKT: Overexpressed	NTRK1: Mutation (SNP) - p.Arg220Gln,MET: Mutation (SNP) - p.Gly937Ser,FLT3: Mutation - p.Val186Leu,KMT2D: Mutation - p.Asp1549frameshift, CDK6: Mutation - p.Ser155Gly				
Mammary Carcinoma	mammary tissue	138	No	Rapamycin, Trametinib	no	0	74							
Mammary Carcinoma	right, #2 mammary gland	236	No	Lapatinib, Trametinib, Vorinostat	yes	1	172		RAS/RAF: Overexpressed ,PTEN: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed	KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	1 Additional Findings of Importance: KMT2C	5 Actionable Findings: CDK4, EGFR, ERBB2, MEK1/2, MYC	1. Lapatinib (EGFR/ERBB 2 inhibitor) - 5-10 mg/kg/day PO 2. Trametinib (MEK inhibitor) -	1. Commonly altered gene family in human malignancies (KMT)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
									d - CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed			10 Additional Findings of Importance : . AKT, BCL6, CCND1, COX2, GLUT1, HIF1a, JAK1, JAK2, PTEN, RAS/RAF	0.02-0.03 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 6. Biomarkers associated with generalized chemo-resistance	
Mammary Carcinoma	left and right mammary chain	21	No	Vorinostat		0	0	SETD2: Mutation - p.Arg1060Cys,NOTCH1: Stop Gained - p.Arg2324*		ROS1: Mutation (SNP) - p.Thr2260Met,KMT2C: Mutation (SNP) - p.His906Tyr,ALK: Stop Gained - p.Gly1616*				
Mammary Carcinoma	Left caudal unilateral mastectomy		No		yes	1								

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Mammary Carcinoma	2nd Left Mammary Gland		No		no	0		mTOR: Mutation - p.Asp1376Glu		P53: Mutation - p.Ser231Tyr,CREBBP : Stop Gained - p.Arg1350*,CDKN2A: Mutation - p.His32Tyr	1 Actionable Findings: mTOR 3 Additional Findings: CDKN2A, CREBBP, P53			1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Gene involved in cell cycle regulation (CDKN2A) 4. Feature of malignant transformation (CREBBP).
Mammary Carcinoma	Left axillary		No			0								

Table 22: Treatment of Lymphoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Lymphoma	Skin	174	No		yes	1					
Lymphoma	multicentric	250	No		yes	1					
Lymphoma	Lymph Nodes	359	No	Apoquel	yes	1	3				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Lymphoma	skin	4	No	Trametinib	no	0	3				
Lymphoma	lymph nodes	35	No		no	0		7 Additional Findings of Importance: ATRX, CREBBP, KDR, KMT2C, KMT2D, NOTCH1, ROS1	3 Actionable Findings: CDK4, JAK1, MYC 6 Additional Findings of Importance: AKT, STAT1, ERCC1/2, MGMT, BRCA1/2, PGP	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Apoquel (JAK1 inhibitor) - dose per label 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Potential tumor sensitivity to alkylating agents and platinum based agents.	1. Potentially oncogenic receptor (KDR). 2. Commonly altered gene family in human malignancies (KMT). 3. Feature of malignant transformation (CREBBP). 4. Canine single nucleotide polymorphism (SNP).
Lymphoma	right cervical lymph node	298	No	Vorinostat	yes	1	3	1 Actionable Findings: CDK4 6 Additional Findings of Importance: P53, PARP1, ARID1A, KMT2C, ROS1 (2)	1 Actionable Findings: CDK4, JAK1, MEK2, MYC 4 Additional Findings of Importance: RRM2, TOP2A, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Apoquel (JAK1 inhibitor) - dose per label 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Potential tumor sensitivity to alkylants and platinum chemotherapy agents 6. Potential tumors resistance to doxorubicin	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Mutation of well described tumor suppressor gene (P53). 3. Mutation of gene normally involved in DNA repair (PARP1) 4. Canine single nucleotide polymorphism (SNP).
Lymphoma	na	545	No	Ibrutinib	yes	1	1				
Lymphoma	Liver, GI	2	No			0					
Lymphoma	spleen, lnns, bone marrow, blood, liver	306	No		yes	1					
Lymphoma	Oral cavity	346	Yes	Trametinib	yes	1	19	1 Actionable Findings: NF1 9 Additional Findings: ALK, BCL6, BRCA2, FGFR2IIIC, PTPRD, SMARC4, KMT2D, NOTCH1, ROS1			1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Tyrosine kinase receptor (ALK) 3. Transcriptional repressor in B-cell lymphocytes (BCL6) 4. Tumor suppressor gene, potential sensitivity to platin based agents (BRCA2) 5. Fibroblast growth factor receptor (FGFR2) 6. Protein tyrosine

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											phosphatase family (PTPRD) 7. Component of SWI/SNF protein complexes (SMARCA4) 8. Canine single nucleotide polymorphism (SNP).
Lymphoma	Left popliteal	785	No		yes	1					
Lymphoma	Peripheral lymph node, left submandibular	58	No	Ibrutinib	yes	1	16				
Lymphoma	Peripheral lymph node	63	No	Rapamycin, Trametinib, Lomustine	yes	1	42				
Lymphoma	CNS, GI, Ocular	212	No	Trametinib, Rapamycin, Cytarabine	yes	1	96				
Lymphoma	right axilla	194	No	Trametinib	yes	1	99				
Lymphoma	Lymphnode	642	No	Trametinib, Apoquel, Vorinostat, Rapamycin, Ibrutinib	yes	1	175				
Lymphoma	lymph node	306	No	Vorinostat, Apoquel	yes	1	54	3 Additional Finding of Importance: KMT2C, ALK, P53	2 Actionable Findings: JAK1, MYC 5 Additional Findings: STAT1, ERCC1/2, MGMT, PGP, RRM1/2	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Apoquel (JAK inhibitor) - dose per label 3. Potential tumor sensitivity to platin based and alkylating agents. 4. Potential tumor sensitivity to gemcitabine.	1. Commonly altered gene family in human malignancies (KMT). 2. Tyrosine kinase receptor (ALK). 3. Mutation of well described tumor suppressor gene (P53).
Lymphoma	Right popliteal lymph node	304	No	Trametinib, Vorinostat, Dasatinib	yes	1	29	6 Additional Findings of Importance: BRAF, ARID1A, KMT2C, IDH1, NOTCH1, PDGFRB	3 Actionable Findings: CDK4, MEK2, MYC 4 Additional Finding of Importance: TOP2A, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Potential sensitivity to anthracyclines, platin based or alkylating agents.	1. Mutated gene family commonly seen in human malignancies (KMT2C). 2. Previously identified canine SNP.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Lymphoma	submandibular lymph node	182	No	Vorinostat, Ibrutinib	yes	1	51	1 Additional Finding of Importance: MET	3 Actionable Findings: CDK4, JAK1, MYC 9 Additional Finding of Importance: AKT, BCL6, COX2, JAK2, HIF1a, RRM2, ERCC1/2, MGMT, PGP	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Apoquel (JAK1 inhibitor) - dose per label 4. Potential sensitivity to platin based and alkylating agents. 5. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs). 6. Potential tumor resistance to gemcitabine.	1. Previously identified canine single nucleotide polymorphism (SNP).
Lymphoma		222	No	Ibrutinib	yes	1	66	2 Additional Findings of Importance: FBXW7, P53	7 Additional Findings of Importance: AKT, COX2, BRCA1/2, ERCC1/2, MGMT, PGP, RRM1/2	1. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 2. Potential tumor sensitivity to chemotherapy with alkylating agents, gemcitabine, and/or platinum based agents.	1. Tumor suppressor gene (FBXW7) 2. Mutation of tumor suppressor gene (P53)
Lymphoma	pharyngeal mass	75	No	Vorinostat	no	0	56	4 Additional Findings of Importance: CREBBP, KMT2C(2), P53	2 Actionable Findings: CDK4, MYC 7 Additional Findings of Importance: DHFR, HIF1a, RRM2, TYMS, BRCA1/2, ERCC1/2, MGMT	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/day/every other day PO 2. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor sensitivity to 5FU, alkylating agents and/or platin based agents 5. Potential tumor resistance to gemcitabine	1. Feature of malignant transformation (CREBBP) 2. Commonly altered gene family in human malignancies (KMT) 3. Previously identified canine single nucleotide polymorphism (SNP)
Lymphoma	peripheral lymphadenopathy	112	No	Rapamycin, Dasatinib	yes	1	0	4 Additional Findings of Importance: FGFR2IIIC, KMT2D(2), VEGFβ	1 Actionable Findings: CDK4 10 Additional Findings of Importance: DHFR, HIF1a, JAK1,	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Biomarkers associated with generalized chemo-resistance 3. Potential tumor resistance to gemcitabine 4. Potential tumor sensitivity to	1. Fibroblast growth factor receptor 2 (FGFR2) 2. Commonly altered gene family in human malignancies (KMT) 3. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
									RRM2, TOP2A, TYMS, BRCA1/2, ERCC1/2, MGMT, PGP	5'FU, doxorubicin, alkylating agents and/or platin based agents	
Lymphoma	Esophagus	61	No		no	0		1 Actionable Findings: KIT 5 Additional Findings of Importance: EGFR, FGFR3(2), KMT2C, RB1	2 Actionable Findings: CDK4, MEK1/2 5 Additional Findings of Importance: AKT, HIF1a, MDM2, PTEN, RRM2	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor resistance to gemcitabine.	1. Imatinib (KIT inhibitor) - 10 mg/kg/day PO 2. Toceranib (KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Proliferation protein kinase receptor (EGFR) 4. Fibroblast growth factor receptor (FGFR) 5. Commonly altered gene family in human malignancies (KMT) 6. Tumor suppressor gene (RB1) 7. Previously identified canine single nucleotide polymorphism (SNP).
Lymphoma	jejunum	99	No	Apoquel, Trametinib, Vorinostat	yes	1	122	5 Actionable Findings: BRAF, PTEN, PDGFRβ, SETD2(2) 17 Additional Findings of Importance: JAK1, ATRX, P53, RTP2, FGFR2IIIC, RET, KMT2D, FLT3(2), FGFR1, KDR, PDGFRα, PTPRD(2), ROS1(3)	5 Actionable Findings: CDK4, EGFR, JAK1, MEK1/2, PDGFR 8 Additional Findings of Importance: AKT, BCL6, JAK2, MDM2, RAS/RAF, VEGF, ERCC1/2, MGMT	1. Trametinib (MEK1/2 inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 3. Apoquel (JAK inhibitor) - dose per label 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO 6. Potential tumor resistance to doxorubicin which may be re-sensitized with Rapamycin. 7. Potential tumor sensitivity to alkylating agents and platins. 8. Intracellular signaling via MAPK/RAS/RAF/ERK and AKT expression reflected RTKs activity.	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Commonly altered gene family in human malignancies (KMT). 4. Potentially oncogenic receptor family (FGFR). 5. Mutation of well described tumor suppressor gene (P53).
Lymphoma	skin	170	No		yes	1					

Table 23: Treatment of Histiocytic Sarcoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations	CST Potential Initial Clinical Approach
Histiocytic Sarcoma	spleen (splenectomy), bone marrow, liver	144	No	Vorinostat, Trametinib	yes	1	6					ATM: Mutation - CST,MEK1/2: Overexpressed - CST	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO
Histiocytic Sarcoma	Hilar lymph node and lung	55	No	Vorinostat	yes	1							
Histiocytic Sarcoma	spleen, right middle lung lobe, perirenal LN, SQ dorsal cervical	28	No	Trametinib, Rapamycin	yes	1	2						
Histiocytic Sarcoma	spleen	36	No			0		4 Additional Findings of Importance: PARP1, IDH1, NOTCH1, ROS1	2 Actionable Findings: CDK4, MEK2 10 Additional Findings of Importance: AKT, CCND1, HIF1a, JAK1, MDM2, PTEN,	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor sensitivity to alkylating agents	1. DNA damage repair gene (PARP1) 2. Previously identified canine single nucleotide polymorphism (SNP)		

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations	CST Potential Initial Clinical Approach
									RRM2, ERCC1/2, MGMT, PGP	5. Potential tumor resistance to gemcitabine and doxorubicin.			
Histiocytic Sarcoma	left knee joint capsule	50	Yes		yes	1							
Histiocytic Sarcoma	Spleen, Omentum	40	No			0		3 Additional Findings of Importance: BRCA2, P53, PDGFRβ	2 Actionable Findings: CDK4, MEK2 16 Additional Findings of Importance: AKT, BCL-XL, GLUT1, HIF1a, JAK1, JAK2, MDM2, PTEN, RAS, RRM2, STAT1, VEGF, BRCA1/2, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor sensitivity to alkylating agents 6. Potential tumor resistance to gemcitabine	1. Tumor supressor gene (BCRA2) 2. Mutation of well described tumor suppressor gene (P53) 3. Previously identified canine single nucleotide polymorphism (SNP)		
Histiocytic Sarcoma	Lymph nodes (external/ internal), likely spleen	135	No			0							
Histiocytic Sarcoma	Right Cranial Lung Lobe	176	No		yes	1							
Histiocytic Sarcoma	left stifle	274	Yes	Vorinostat, Crizotinib, Trametinib	yes	1	220						
Histiocytic Sarcoma	liver and omentum	142	No	Rapamycin, Vorinostat, Erlotinib, Trametinib	yes	1	76						

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations	CST Potential Initial Clinical Approach
Histiocytic Sarcoma	liver and spleen	63	No	Trametinib	yes	1	42						
Histiocytic Sarcoma	L stifle, L medial iliac and visceral lymph nodes	4154	Yes	Rapamycin, Dasatinib	yes	1	0						
Histiocytic Sarcoma	R cranial lung lobe	1039	No	Dasatinib, Rapamycin	yes	1	93						
Histiocytic Sarcoma	lungs and node	684	No	Trametinib	yes	1	47						
Histiocytic Sarcoma	lobulated spleen with ill-defined hypoechoic nodules & coarse echotexture	103	No	Trametinib, Rapamycin	no	0	65	1 Additional Finding of Importance: P53	4 Actionable Findings: CDK4, JAK1, MEK1/2 10 Additional Findings of Importance: AKT, E2F1, HIF1a, JAK2, MDM2, RAS/RAF, RRM1/2, STAT1, TOP2A	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Apoquel (JAK inhibitor) - dose per label 4. Intracellular signaling via JAK/STAT pathway 5. Potential tumor sensitivity to anthracyclines.	1. Mutation of well described tumor suppressor gene (P53).		
Histiocytic Sarcoma	Left Thorax	120	No	Vorinostat, Trametinib	yes	1	72	5 Additional Findings of Importance: BRCA1(2), FGFR2IIIC, KMT2C, P53	5 Actionable Findings: CDK4, JAK1, MEK1/2, MYC, PDGFR 14 Additional Finding of Importance: AKT, BCL-XL, BCL6, GLUT1, HIF1a, JAK2, MDM2, RAS/RAF,	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 6. Apoquel (JAK1 inhibitor) - dose per label 7. Potential tumor sensitivity to alkylating agents and	1. Mutation of well described tumor suppressor gene P53. 2. Tumor supressor gene (BRCA1/2). 3. Previously identified canine SNP.		

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations	CST Potential Initial Clinical Approach
									STAT1, TOP2A, ERCC1/2, MGMT, PGP	anthracyclines. 8. Biomarkers associated with generalized chemoresistance. 9. Potential tumor sensitivity to non-steroidal anti-inflammatory drugs (NSAIDs).			
Histiocytic Sarcoma	right rear leg, caudal distal femur	403	No	Rapamycin, Trametinib	yes	1	32	3 Additional Findings of Importance: BRCA2(2), JAK3	3 Actionable Findings: CDK4, MEK1/2, JAK1 10 Additional Finding of Importance: AKT, GLUT1, HIFa, MDM2, RAS/RAF, RRM1/2, STAT1, VEGF, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Apoquel (JAK1 inhibitor) - dose per label 4. Potential tumor sensitivity to alkylating agents. 5. Potential tumor resistance to doxorubicin and gemcitabine. 6. Biomarkers associated with generalized chemo and radiation resistance.	1. Mutation of well described tumor suppressor gene (BRCA2). 2. Tyrosine kinase mediated intracellular signal transduction (JAK3).		
Histiocytic Sarcoma	Multiple LNs (Inguinal LN biopsied)	50	No	Trametinib	no	0	1	3 Additional Finding of Importance: BRCA2, MET, KMT2D	3 Actionable Findings: JAK1, MEK1/2, MYC 10 Additional Findings of Importance: AKT, BCL6, BCL-XL, GLUT1, HIF1a, JAK2, MDM2, RAS/RAF, STAT1, VEGF	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Apoquel (JAK inhibitor) - dose per label 4. Potential tumor resistance to doxorubicin. 5. Biomarkers associated with generalized chemo and radiation resistance. 6. Intracellular signaling via JAK/STAT pathway.	1. Mutation of well described tumor suppressor gene (BRCA2). 2. Commonly altered gene family in human malignancies. 3. Previously identified canine single nucleotide polymorphism (SNP).		
Histiocytic Sarcoma	right eye	246	No	Trametinib, Rapamycin, Vorinostat	yes	1	216	1 Actionable Findings: ATM	2 Actionable Findings: CDK4, MEK1/2	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC/CDK4	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO		

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations	CST Potential Initial Clinical Approach
								8 Additional Findings of Importance: BRCA1, ROS1(2), FLT3, IDH1, JAK2, KMT2D(2)	13 Additional Findings of Importance: AKT, COX2, GLUT1, HIF1a, JAK1, JAK2, RAS, RRM2, STAT1, TOP2A, ERCC1/2, MGMT, PGP	inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 4. Biomarkers associated with generalized chemo-resistance 5. Potential tumor resistance to gemcitabine 6. Potential tumor sensitivity to doxorubicin, alkylating agents and/or platin based agents	2. Tumor supressor gene (BRCA1) 3. Tyrosine kinase insulin receptor (ROS1) 4. Previously identified canine single nucleotide polymorphism (SNP)		
Histiocytic Sarcoma	Spleen	162	No	Trametinib, Rapamycin	yes	1	106	4 Additional Findings of Importance: CREBBP, P53(2), CDKN2A	3 Actionable Findings: CDK4, MEK1/2, MYC 11 Additional Findings of Importance: AKT, BCL2, JAK1, JAK2, RRM2, STAT1, VEGF, BRCA1/2, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/day every other day PO 4. Potential tumor resistance to gemcitabine 5. Potential tumor sensitivity to methotrexate, platin agents and/or alkylating agents	1. Feature of malignant transformation (CREBBP) 2. Mutation of well described tumor suppressor gene (P53) 3. Previously identified canine single nucleotide polymorphism (SNP) in healthy canines.		
Histiocytic Sarcoma	Dorsal neck are with prescapular LNN involvement	47	No	Vorinostat	no	0	13	5 Additional Findings: CREBBP, P53, RET, ABL1, BRAF			1. Feature of malignant transformation (CREBBP) 2. Potential resistance to anthracylines, alkylating, antimetabolites and platin based agents (P53) - consider HDAC inhibitor 3. Tyrosine kinase receptor (RET) - can consider RTK inhibitor like toceranib.		

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications	CST Alterations	CST Potential Initial Clinical Approach
											4. Canine single nucleotide polymorphism (SNP).		
Histiocytic Sarcoma	Right cranial lung lobe	156	No	Rapamycin, Trametinib	yes	1	95	6 Additional Findings of Importance: KMT2C, KMT2D, NOTCH1, P53, VEGFB, VEGFB	5 Actionable Findings: CDK4, JAK1, MEK1/2, mTOR, MYC 10 Additional Findings of Importance: AKT, BCL2, GLUT1, HIF1a, JAK2, MDM2, PTPN11, RAS/RAF, STAT1, TOP2A, VEGF	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Apoquel (JAK inhibitor) - dose per label 6. Biomarkers associated with generalized chemotherapy and radiotherapy resistance. 7. Potential tumor sensitivity to anthracyclines (TOP2A)	1. Mutation of well described tumor suppressor gene (P53). 2. Commonly altered gene in human malignancies (KMT). 3. Canine single nucleotide polymorphisms (SNPs).		

Table 24: Treatment of Hepatocellular Carcinoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hepatocellular Carcinoma	Left Medial	28	No		no	0									

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (Yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
	Liver Lobe														
Hepatocellular Carcinoma	Liver	386	No			0		MYC: Overexpressed ,MEK2: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,PTEN: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Ile133Val,FLT1: Mutation (SNP) - p.Arg856Gln,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Gly59Ser	4 Additional Findings of Importance: CREBBP, KMT2C, FLT1, ROS1	2 Actionable Findings: MEK2, MYC 9 Additional Findings of Importance: AKT, CCDN1, COX2, PTEN, VEGF, BRCA1/2, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 4. Potential tumor sensitivity to alkylating and/or platin based chemotherapy	1. Transcription activating gene (CREBBP) 2. Commonly altered gene family in human malignancies (KMT) 3. Previously identified canine single nucleotide polymorphism (SNP).
Hepatocellular Carcinoma	Multiple liver lobectomies - with now presumed multiple target lesions on	599	No	Rapamycin, Trametinib	no	0	88	MYC: Overexpressed ,MET: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST	SETD2: Mutation - p.Tyr1268Phe	Rapamycin: ,RRM1/2: Underexpressed ,MGMT: Underexpressed ,RAS/RAF: Overexpressed ,PROX1:	KMT2C: Mutation - p.3163_3164insAsnLys	1 Actionable Finding: SETD2 1 Additional Finding of Importance: KMT2C	5 Actionable Findings: KDR, MEK1/2, MET, MYC 11 Additional Findings of Importance: BCL-XL,	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR inhibitor) - 10	1. Vorinostat (HDAC inhibitor) - 45 mg/kg/every other day PO 2. Commonly

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
	abdominal ultrasound and cytology is consistent with presumed hepatocellular carcinoma.									Overexpressed ,PGP: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,COX2: Overexpressed ,BCL-XL: Overexpressed			COX2, HIF1a MDM2, PGP, PROX1, RAS/RAF, MGMT, RRM1/2	mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 45 mg/kg/every other day PO 4. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 5. Potential therapeutic benefit from NSAIDs. 6. Biomarkers associated with generalized chemoresistance including doxorubicin and the small molecule inhibitor, Sorafenib. 7. Potential tumor sensitivity to gemcitabine and/or alkylating agents. 8. Intracellular signaling via	altered gene family in human malignancies (KMT).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														MAPK/ERK pathway.	
Hepatocellular Carcinoma	liver	839	No		yes	1		MYC: Overexpressed ,MET: Overexpressed ,MEK2: Overexpressed		ERCC1/2: Underexpressed ,MDM2: Overexpressed ,COX2: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,FLT3: Mutation - p.Val186Leu,FLT3: Mutation - p.Asp748Asn	3 Additional Findings of Importance: FLT3 (2), ROS1	3 Actionable Findings: MEK2 (MAP2K2), MET, MYC 4 Additional Findings of Importance: COX2, MDM2, ERCC1/2	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Crizotinib (MET inhibitor) - 1 mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 45 mg/kg/every other day PO 4. Potential therapeutic benefit of NSAIDs. 5. Potential tumor sensitivity to platinum based therapies and/or radiation therapy. 6. Potential tumor resistance to chemotherapies such as doxorubicin.	1. Novel mutation identified in the protein tyrosine kinase domain (FLT3). 2. Canine single nucleotide polymorphisms (SNPs).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (Yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hepatocellular Carcinoma	Liver	285	No	Vorinostat, Rapamycin	no	0	250	MYC: Overexpressed	MTOR: Mutation - p.Ser2216Phe	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,COX2: Overexpressed ,CCND1: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn,KMT2C: Mutation (SNP) - p.His906Tyr,JAK2: Mutation - p.Phe560Val,CREBBP: Mutation - p.Ala785Asp	1 Actionable Findings: mTOR 4 Additional Findings of Importance: CREBBP, JAK2, KMT2C, MET	1 Actionable Findings: MYC 7 Additional Findings of Importance: CCND1, COX2, BRCA1/2, ERCC1/2, MGMT, PGP, RRM1/2	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 3. Potential tumor sensitivity to chemotherapy with alkylating and/or platinum based agents. 4. Potential tumor sensitivity to gemcitabine.	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Transcription activating gene (CREBBP) 3. Tyrosine kinase involved in cytokine intracellular signal transduction (JAK2) 4. Previously identified canine single nucleotide polymorphism (SNP).
Hepatocellular Carcinoma	Liver	62	No	Vorinostat	no	0	2		P53: Stop Gained - p.Gly254*		ROS1: Mutation (SNP) - p.Arg1606His	2 Mutations Identified: P53, ROS1			POTENTIAL CLINICAL SIGNIFICANCE P53: Potential resistance to anthracyclines, alkylating, antimetabolit

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Total Days on Targeted Drugs	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															es and platin based agents. Consider HDAC inhibitor. UNKOWN CLINICAL SIGNIFICANCE ROS1: Previous identified as a SNP in canine.
Hepatocellular Carcinoma		79	No		yes	1					ROS1: Mutation (SNP) - p.Arg1237Gln,JAK2: Mutation (SNP) - p.Thr514Asn,KMT2C: Mutation - p.Ala4122Ser				

Table 25: Treatment of Hemangiosarcoma

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alteration	Potentially Clinically Significant Findings	Other RNA Alteration	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Spleen and Liver	21	No		yes	1		MEK2: Overexpressed ,KDR: Overexpressed - CST,CDK4: Overexpressed		RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,AKT: Overexpressed			3 Actionable Findings: CDK4, KDR, MEK2 8 Additional Findings of Importance: AKT, HIF1a, JAK1, VEGF, BRCA 1/2, MGMT, PGP, RRM1/2	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance 6.	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														Potential tumor sensitivity to gemcitabine, alkylating agents and/or platin based agents	
Hemangiosarcoma	spleen, liver omentum	15	No		no	0									
Hemangiosarcoma	Spleen/Liver	45	No		yes	1			EGFR: Mutation - p.Pro236Leu,PDGFRa: Mutation - p.Arg696His		RTP2: Mutation (SNP) - p.His97Tyr,BRCA2: Mutation - p.Met3332_Lys3333insIleLys				
Hemangiosarcoma	Spleen	209	No		yes	1			NOTCH1: Mutation - p.Val2035Leu		RTP2: Mutation (SNP) - p.His97Tyr,NOTCH1: Mutation (SNP) - p.Ala2121Thr,KMT2D: Mutation - p.Lys803Glu,KMT2D: Mutation - p.Leu934Pro				
Hemangiosarcoma	Spleen	115	No		yes	1									
Hemangiosarcoma	Spleen	98	No	Rapamycin, Imatinib	yes	1	12								
Hemangiosarcoma	spleen and liver	13	No		yes	1									
Hemangiosarcoma	spleen	204	No	Rapamycin, Imatinib	no	0	22								
Hemangiosarcoma	Spleen	17	No		no	0									
Hemangiosarcoma	Caudal abdominal mass	300	Yes		yes	1		MYC: Overexpressed ,MEK1/2	SETD2: Mutation - p.Tyr1268Phe	PGP: Underexpressed ,MGMT:	BRAF: Mutation (SNP) - p.Ile322Val	1 Actionable Finding:	4 Actionable Findin	1. Imatinib (KDR/KIT inhibitor) - 10	1. Vorinostat (HDAC inhibitor)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								. . Overexpressed - CST,KIT . . Overexpressed ,KDR: Overexpressed - CST		Underexpressed ,ERCC1/2: Underexpressed ,GLUT1: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed		SETD2 1 Additional Finding of Importance: BRAF	gs: KDR, KIT, MEK1/2, MYC 6 Additional Findings of Importance: AKT, CCND1, GLUT1, ERCC1/2, MGMT, PGP	mg/kg/day PO 2. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Potential tumor sensitivity to platin based and alkylating therapies.	- 30 mg/kg/every other day PO 2. Previously identified canine SNP.
Hemangiosarcoma	Abdominal	258	No	Imatinib, Rapamycin	yes	1	17	MEK1: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine	PGP: Underexpressed	VEGFβ: Mutation (SNP) - Intron variant,VEGFβ: Mutation (SNP) - p.Thr195Ala,P53: Mutation -	1 Actionable	4 Actionable	1. Imatinib (KIT/KDR inhibitor) -	1. Rapamycin
Hemangiosarcoma	withers	57	No		no	0									

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	spleen, liver, lung	395	No	Vorinostat	yes	1	0	,KIT: Overexpressed ,KDR: Overexpressed - CST ,JAK1: Overexpressed - CST	HSA and Human Hotspot)	,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed	p.Tyr115Cys,P53: Stop Gained - p.Glu276*	Findings: PIK3CA 4 Additional Findings of Importance: P53(2), VEGFB(2)	Findings: JAK1, KDR, KIT, MEK1 6 Additional Findings of Importance: HIF1a, PTEN, BRCA 1/2, ERCC 1/2, MGMT, PGP	10 mg/kg/day PO 2. Palladia (KIT/KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Apoquel (JAK1 inhibitor) - dose per label 5. Potential tumor sensitivity to alkylating agents and/or platin based chemotherapy.	(mTOR inhibitor) - 0.1 mg/kg/day PO 2. Mutation of well described tumor suppressor gene (P53) 3. Previously identified canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	spleen and liver; previously muscular	728	Yes		yes	1								1. Toceranib (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 5.	1. Tyrosine kinase receptor (KIT) 2. Previously identified canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	Right lateral thigh	13	No		no	0									
Hemangiosarcoma	Spleen	36	Yes		yes	1		MYC: Overexpressed ,MEK1: Overexpressed ,KIT: Overexpressed ,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		RRM1/2: Underexpressed ,PGP: Underexpressed ,ERCC1/2: Underexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,ROS1: Mutation (SNP) - p.Ile133Val,KIT: Mutation (SNP) - p.Pro20Leu,KIT: Mutation - p.Gln380Arg	4 Additional Findings of Importance: KIT(2), ROS1(2)	6 Actionable Findings: CDK4, JAK1, KDR, KIT, MEK1, MYC 7 Additional Findings of Importance: AKT, CCND1, HIF1a, PTEN, ERCC1/2, PGP, RRM1/2		

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Apoquel (JAK inhibitor) - dose per label 7. Potential tumor sensitivity to gemcitabine and/or platin based chemotherapy.	
Hemangiosarcoma	Spleen, Liver	18	No		yes	1		MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,CDK4: Overexpressed		MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TYMS: Overexpressed ,RRM2:	NOTCH1: Mutation (SNP) - p.Ser1456Asn,P53: Mutation - p.Ser205Arg,N-RAS: Mutation - p.Gly13Arg	3 Additional Findings of Importance: N-RAS, P53, NOTCH 1	3 Actionable Findings: CDK4, KDR, MEK1/2 10 Additional Findings of	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3.	1. Potential dysregulation of MAP kinase signaling protein N-RAS. 2. Mutation of well described tumor suppress

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed ,PTEN: Overexpressed ,JAK1: Overexpressed - CST,HIF 1a: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed			Importance: AKT, BCL-XL, HIF1a, JAK1, PTEN, RRM2, TYMS, BRCA 1/2, ERCC 1/2, MGMT	Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Dasatinib (CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor resistance to gemcitabine 7. Potential tumor sensitivity to 5'FU, alkylating agents and/or platin based	or gene (P53). 3. Single nucleotide polymorphism (SNP) previously identified in health canines.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														chemotherapy	
Hemangiosarcoma	initially cervical LN, currently presumptive metastasis to spleen/liver/lung	181	No		yes	1		MEK1/2: Overexpressed - CST,BCR-ABL Fusion Gene: Overexpressed		RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,PTEN: Overexpressed ,STAT1: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,ERCC1: Overexpressed ,AKT: Overexpressed			2 Actionable Findings: BCR-ABL, MEK1/2 9 Additional Findings of Importance: AKT, ERCC1, HIF1a, JAK1, STAT1, PTEN, MGMT, PGP, RRM1/2	1. Imatinib (BCR-ABL inhibitor) - 10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor resistance to platin based agents 5. Potential tumor sensitivity to gemcitbaine, methotrexate and/or	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														alkylating agents	
Hemangiosarcoma	initially cervical LN, currently presumptive metastasis to spleen/liver/lung	181	No		yes	1		MEK1/2: Overexpressed - CST,BCR-ABL Fusion Gene: Overexpressed		RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,PTEN: Overexpressed ,STAT1: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,ERCC1: Overexpressed ,AKT: Overexpressed			2 Actionable Findings: BCR-ABL, MEK1/2 9 Additional Findings of Importance: AKT, ERCC1, HIF1a, JAK1, STAT1, PTEN, MGMT, PGP, RRM1/2	1. Imatinib (BCR-ABL inhibitor) - 10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor resistance to platin based agents 5. Potential tumor sensitivity to gemcitbaine, methotrexate and/or	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														alkylating agents	
Hemangiosarcoma	Spleen, liver	14	No		yes	1		MYC: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST	PIK3CA: Mutation - p.Thr1025Ala	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed	NOTCH1: Mutation (SNP) - p.Ser1456Asn,MET: Mutation (SNP) - p.Gly937Ser,KMT2D: Mutation - p.Ser855Pro,ATRX: Mutation - p.Ile736fs	1 Actionable Finding s: PIK3CA 4 Additional Findings of Importance: ATRX, KMT2D, MET, NOTCH1	3 Actionable Findings: KDR, MEK1/2, MYC 11 Additional Findings of Importance: AKT, BCL-XL, GLUT1, HIF1a, JAK1, TOP2A, TYMS, ERCC1/2, MGMT, PGP, RRM1/2	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Tumor supressor gene in sarcoma and gliomas (ATRX) 3. Commonly altered gene family in human malignancies (KMT) 4. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														6. Potential tumor sensitivity to 5FU, gemcitabine, doxorubicin, alkylating agents and/or platin based agents	
Hemangiosarcoma	Right shoulder, splenic	44	No		yes	1		KDR: Overexpressed - CST	ATM: Mutation - p.Ala989Val	RRM1/2: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,RAS/RAF: Overexpressed	BRCA1: Mutation (SNP) - p.Gly192Ser,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,BRCA1: Mutation - p.Gly264Asp	1 Actionable Finding s: ATM 3 Additional Findings of Importance: BRCA1(2), KMT2C	1 Actionable Findings: KDR 12 Additional Findings of Importance: COX2, GLUT1, HIF1a, MDM2, JAK1, RAS/RAF, TOP2A,	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs)	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Tumor suppressor gene (BRCA1) 3. Commonly altered gene family in human malignancies (KMT) 4. Previously

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Muscle right rear hip and spleen	68	No	Trametinib, Rapamycin		0	18			,JAK1: Overexpressed - CST,MDM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed			TYMS, BRCA 1/2, ERCC 1/2, MGMT , RRM1/2	4. Biomarkers associated with generalized chemo-resistance 5. Potential resistance to doxorubicin that may be re-sensitized with Rapamycin 6. Potential tumor sensitivity to 5FU, alkylating agents and/or gemcitabine	identified canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	spleen	22	No		unknown	0									
Hemangiosarcoma	Spleen	22	No		yes	1			NOTCH1: Mutation (SNP) - p.Val2035Ile,NOTCH1: Mutation - p.Glu643Lys		ROS1: Mutation (SNP) - p.Thr2260Met,BRCA2: Mutation (SNP) - p.Ile2226Met,BRCA2: Mutation (SNP)	2 Actionable Finding			1. Vorinostat (HDAC inhibitor)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											- p.Ile830Val,RET: Mutation - p.Gly338Ser	s: NOTCH 1(2) 4 Additional Findings: RET, BRCA2(2), ROS1			- 30 mg/kg/every other day PO 2. Tyrosine kinase receptor (RET) - can consider Tocerinib 3. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	Spleen	45	No		yes	1			SETD2: Mutation - p.Tyr1268Phe		NOTCH1: Mutation (SNP) - p.Ser1456Asn,MET: Mutation (SNP) - p.Asp583Asn,CREBBP: Mutation (SNP) - p.Gly2097Ser,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Gly59Ser	1 Actionable Finding: SETD2 5 Additional Findings: CREBBP(2), KMT2C, MET, NOTCH1			1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Feature of malignant transformation (CREBBP) 3. Commonl

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															y altered gene family in human malignancies (KMT) 4. Previously identified canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	Spleen, Liver	35	No		no	0			P53: Mutation - p.Leu182Pro		JAK2: Mutation (SNP) - p.Thr514Asn,TERT: Mutation - p.Gln1102_Gln1103fs,ATRX: Mutation - p.Glu991_Val992fs				
Hemangiosarcoma	Spleen, Liver	35	No		no	0			P53: Mutation - p.Leu182Pro		JAK2: Mutation (SNP) - p.Thr514Asn,TERT: Mutation - p.Gln1102_Gln1103fs,ATRX: Mutation - p.Glu991_Val992fs				
Hemangiosarcoma	Spleen and liver	52	No		yes	1									
Hemangiosarcoma	spleen	99	No		yes	1			FLT3: Mutation - p.Asp748Asn,FLT3: Mutation - p.Val186Leu,ATM: Mutation - p.Gly2186Arg		VEGFC: Mutation - p.Ala147Thr,ROS1: Mutation (SNP) - p.Thr2260Met,PARP1: Mutation (SNP) - p.Ala451Glu,KMT2C: Mutation - p.Pro4236Leu				
Hemangiosarcoma	Right kidney/perirenal mass	98	No	Rapamycin	yes	1	3								

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	spleen	44	No	Rapamycin	yes	1	26								
Hemangiosarcoma	Left caudal thigh	31	Yes	Rapamycin, Vorinostat		0	19		SETD2: Mutation - p.Lys1800Asn,PIK3CA: Mutation - p.His1047Leu (Canine HSA and Human Hotspot) ,P53: Mutation - p.Gly254Glu,P53: Mutation - p.Cys230Arg,BRCA2: Mutation - p.Met3332Lys		NOTCH1: Mutation (SNP) - p.Ala2121Thr,MET: Mutation (SNP) - p.Asp583Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser,BRCA2: Mutation (SNP) - p.Asn2929Asp,BRAF: Mutation (SNP) - p.Ile322Val,ARID1A: Mutation - p.Arg728Trp				
Hemangiosarcoma	spleen, liver	126	No	Vorinostat		0	0				KMT2D: Mutation - p.Ser744Pro				
Hemangiosarcoma	Spleen	48	No	Rapamycin		0	0		mTOR: Mutation - p.Asp1376Glu		NOTCH1: Mutation (SNP) - p.Ala2121Thr,KMT2D: Mutation (SNP) - p.Pro876Leu,BRAF: Mutation (SNP) - p.Ile322Val				
Hemangiosarcoma	Spleen, now liver metastasis	78	No	Rapamycin	yes	1	0		PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot) ,P53: Mutation - p.Tyr150Ser		MET: Mutation (SNP) - p.Gly937Ser,ATRX: Stop Gained - p.Lys971*				
Hemangiosarcoma	Spleen and Liver	30	Yes			0			BRCA2: Mutation - p.Met3332Lys,mTOR: Mutation - p.Tyr2072Ser,P53: Mutation - p.Arg238Trp		ABL1: Mutation (SNP) - p.Leu830Phe,FLT3: Mutation (SNP) - p.Thr142Ile,MET: Mutation (SNP) - p.Asp583Asn,ROS1: Mutation (SNP) - p.Thr2260Met,FGFR1: Mutation - p.Asn295His,ARID1A: Mutation - p.Ala822Thr				
Hemangiosarcoma	Spleen and Liver	30	Yes			0			P53: Mutation - p.Arg238Trp,mTOR: Mutation - p.Tyr2072Ser,BRCA2: Mutation - p.Met3332Lys		ROS1: Mutation (SNP) - p.Thr2260Met,MET: Mutation (SNP) - p.Asp583Asn,FLT3: Mutation (SNP) - p.Thr142Ile,FGFR1: Mutation - p.Asn295His,ARID1A: Mutation - p.Ala822Thr,ABL1: Mutation (SNP) - p.Leu830Phe				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Spleen	43	No		yes	1									
Hemangiosarcoma	spleen and liver	34	No	Rapamycin, Dasatinib	yes	1	0								
Hemangiosarcoma	Right ventral abdomen	1274	No	Trametinib	yes	1	0	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2. . Overexpressed - CST,JAK1: Overexpressed - CST,ERBB2 (HER2/neu): Overexpressed ,EGFR: Overexpressed - CST,CDK4: Overexpressed		RRM1f2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,RAF: Overexpressed ,PTEN: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,KMT2C: Mutation (SNP) - p.His906Tyr	2 Additional Findings of Importance: KMT2C, ROS1	7 Actionable Findings: CDK4, EGFR, ERBB2, JAK1, MEK1/2, MYC, PDGFR 10 Additional Findings of Importance: AKT, GLUT1, HIF1, JAK2, PTEN, RAF, ERCC1/2, MGMT, PGP,	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Lapatinib (EGFR/ERBB2 inhibitor) - 5-10 mg/kg/day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 5. Toceranib (PDGFR	1. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
													RRM1/2	inhibitor) - 2.5-3.25 mg/kg/every other day PO 6. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 7. Apoquel (JAK inhibitor) - dose per label 8. Biomarkers associated with generalized chemo-resistance 9. Potential tumor sensitivity to gemcitabine, alkylating agents and/or platin based	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														chemotherapy	
Hemangiosarcoma	Spleen	866	No		yes	1			ATM: Mutation - p.V1982 splice		MET: Mutation (SNP) - p.Asp583Asn,NTRK3: Mutation - p.304 splice				
Hemangiosarcoma	rt triceps	215	No		no	0			EGFR: Mutation - p.Pro236Leu,NOTCH1: Mutation - p.Ser1459Asn,P53: Mutation - p.Cys171*		FBXW7: Mutation - p.200 splice,NTRK3: Mutation - p.304 splice				
Hemangiosarcoma	Spleen/Liver	146	No	Vorinostat, Trametinib	yes	1	17		PDGFRβ: Inframe Insertion - Ala1064_Asp1065insAlaAsp,NOTCH1: Mutation - p.Val2035Leu		KMT2C: Mutation (SNP) - p.His906Tyr,EGFR: Mutation (SNP) - p.Arg202Gln,FAT1: Mutation - p.Ile2852Met,VEGFβ: Mutation (SNP) - p.Thr195Ala,VEGFβ: Mutation (SNP) - p.Leu146Val,BRCA2: Mutation - p.Met3332_Lys3333insIleLys,KMT2D: Mutation - p.Pro895_Arg904del,PDGFRβ: Mutation (SNP) - p.Arg705Cys,NTRK1: Mutation (SNP) - p.Arg220Gln				
Hemangiosarcoma	Left hind leg	435	No	Vorinostat, Chlorambucil, Imatinib, Trametinib, Toceranib	yes	1	304				KMT2C: Mutation - p.Gln3726_Pro3727fs,KMT2D: Mutation - p. Gln2847*, KDR: Mutation - p.Ala594Val,NOTCH1: Mutation - p.Val2035Leu				
Hemangiosarcoma	spleen	80	No	Vorinostat, Rapamycin, Imatinib	yes	1	22		EGFR: Mutation - p.Pro236Leu,mTOR: Mutation - p.Asp1376Glu,PDGFRβ: Inframe Insertion - Ala1064_Asp1065insAlaAsp		KMT2C: Mutation - p.Gln3726_Pro3727fs,KMT2D: Mutation - p. Gln2847*,FAT1: Mutation - p.Ser421Phe,BRCA2: Mutation - p.Met3332_Lys3333insIleLys,SETD2: Mutation - p. Tyr1268Phe,KMT2D: Mutation - p.Met1832Ile,KMT2D: Mutation - p.Val4565Ala,BRCA1:				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											Mutation (SNP) - p.Gly192Ser,NOTCH1: Mutation (SNP) - p.Ala2121Thr,BRCA1: Mutation - p.Gly451Asp,ABL1: Mutation (SNP) - p.Ala925Thr				
Hemangiosarcoma	Spleen	260	No	Toceranib, Crizotinib, Deramaxx	yes	1	216		EGFR: Mutation - p.Pro236Leu,PTEN: Mutation - p.Arg108Gln,P53: Mutation - p.Gly254Glu,P53: Mutation - p.Cys163Tyr		MET: Mutation (SNP) - p.Asp583Asn,PTPRD: Mutation - p.His1376Gln,KMT2C: Mutation (SNP) - p.His906Tyr,EGFR: Mutation (SNP) - p.Arg202Gln,NOTCH1: Mutation (SNP) - p.Ser1456Asn				
Hemangiosarcoma	SQ mass L scapular region; diffuse pulmonary metastasis, liver and spleen involvement	56	No	Imatinib	yes	1	18		P53: Mutation - p.Ala64fs,PDGFRβ: Inframe Insertion - Ala1064_Asp1065insAlaAsp,NOTCH1: Mutation - p.Val2035Leu,P53: Mutation - p.Arg325Cys		MET: Mutation (SNP) - p.Asp583Asn,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,KMT2D: Mutation - p.Pro4345_Gln4346del,NTRK3: Mutation (SNP) - p.Ser42Asn,RTP2: Mutation (SNP) - p.His97Tyr,APC: Mutation (SNP) - p.Ala1298Thr,NOTCH1: Mutation (SNP) - p.Thr2278Pro				
Hemangiosarcoma	Spleen	454	No	Vorinostat, Dasatinib, Rapamycin	no	0	264		PDGFRβ: Inframe Insertion - Ala1064_Asp1065insAlaAsp,NOTCH1: Mutation - Val2035Leu		RTP2: Mutation (SNP) - p.His97Tyr,BRCA2: Mutation - p.Met3332_Lys3333insIleLys,CREBBP: Mutation - p.Leu1093*,TERT: Mutation - p.Ala1068_Tyr1069fs				
Hemangiosarcoma	spleen	409	No		no	0			NOTCH1: Mutation - p.Val2035Leu,PDGFRβ: Inframe Insertion - Ala1064_Asp1065insAlaAsp,BRAF: Mutation - p.Asn569Tyr		NOTCH1: Mutation (SNP) - p.Ser1456Asn,BRCA2: Mutation - p.Met3332_Lys3333insIleLys,KMT2C: Mutation (SNP) - p.His906Tyr,KMT2D: Mutation - p.Pro4345_Gln4346del,KMT2C: Mutation - p.Gln3726_Pro372fs				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Liver, subcutaneous and lung nodules	60	No	Trametinib, Toceranib, Rapamycin, Imatinib	no	0	41	PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	PGP: Underexpressed ,ERCC1/2: Underexpressed ,PIK3CA: Overexpressed ,MGMT: Overexpressed ,MDM2: Overexpressed ,AKT: Overexpressed	P53: Mutation - Inframe Deletion p.219-221,RTP2: Mutation (SNP) - p.His97Tyr,CREBBP: Inframe Deletion - p. Pro2046_Gln2047del	1 Actionable Finding: PIK3CA 1 Additional Finding of Importance: P53	3 Actionable Findings: KDR, MEK1/2, PDGFR 8 Additional Findings of Importance: AKT, BRCA1, MDM2, MGMT, PIK3CA, ERCC1/2, PGP	1. Imatinib (KDR/PDGFR inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR/PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 5. Potential tumor resistance to doxorubicin that may be re-sensitized with	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Mutation of well described tumor suppressor gene P53.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														Rapamycin. 6. Potential tumor resistance to alkylating agents. 7. Potential tumor sensitivity to platinum-based agents.	
Hemangiosarcoma	Spleen	123	No	Trametinib, Rapamycin	yes	1	38		PDGFRα: Mutation - p.Arg696His,PTEN: Mutation - p.Pro325Arg,P53: Mutation - p.Arg164His		KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,BRCA2: Inframe Insertion - p.Met3332_Lys3333insIleLys,BRCA2: Mutation - p.Pro3213Leu,KMT2D: Mutation - p.Leu990Ser				
Hemangiosarcoma	Primary tumor in the spleen with metastasis to the liver	92	No	Rapamycin	no	0	27								
Hemangiosarcoma	Spleen	172	No	Rapamycin, Vorinostat	yes	1	1003								
Hemangiosarcoma	Spleen	233	No	Imatinib, Rapamycin	no	0	197	CDK4: Overexpressed ,JAK1:	NOTCH1: Mutation - p.Val2035Leu,ATM: Mutation - p.Ala989Val	AKT: Overexpressed ,CCND1:	ROS1: Mutation (SNP) - p.Thr2260Met,ROS1: Mutation (SNP) - p.Arg1606His,BRCA1: Mutation (SNP) - p.Gly192Ser,RTP2: Mutation (SNP) -				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Right body wall	126	No	Rapamycin, Imatinib	yes	1	0	Overexpressed - CST,KDR: Overexpressed - CST,MEK1/2: Overexpressed - CST		Overexpressed ,HIF1a: Overexpressed ,STAT1: Overexpressed ,JAK2: Overexpressed ,BRCA1/2: Underexpressed ,ERCC1/2: Underexpressed ,MGMT: Underexpressed ,PGP: Underexpressed ,COX2: Overexpressed	p.His97Tyr,BRCA2: Mutation - p.Leu2306_Leu2307 deletion,BRCA2: Mutation (SNP) - p.Asn2929Asp,BRCA1: Mutation - p.Gly451Asp,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys				
											RTP2: Mutation (SNP) - p.His97Tyr,JAK3: Mutation (SNP) - p.Ala220Thr,RET: Mutation - Ala465Gly,ALK: Mutation - Gln1174His				
Hemangiosarcoma	liver	99	No		yes	1	10		PDGFRα: Mutation - p.Arg696His,P53: Mutation - Glu259Val		BRCA2: Mutation - p.Leu2306_Leu2307 deletion,PARP1: Mutation (SNP) - p.Ala451Glu,RTP2: Mutation (SNP) - p.His97Tyr,PARP1: Mutation - Ala49Val				
Hemangiosarcoma	caudal right stifle	171	No	Trametinib,	yes	1	85		P53: Mutation - p.Thr243_Ile244fs		ROS1: Mutation (SNP) - p.Ile133Val,RTP2: Mutation (SNP) -				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
				Dasatinib							p.His97Tyr,ATRX: Mutation - Leu1751Ile,PDGFRβ: Mutation (SNP) - p.Glu400Lys				
Hemangiosarcoma	Liver	123	No	Imatinib, Rapamycin	unknown	0	89								
Hemangiosarcoma	Spleen and omentum	119	No		yes	1			PIK3CA: Mutation - p.Gly1049Arg,NOTCH1: Mutation - p.Val2035Leu,P53: Mutation - p.Glu274Val,P53: Mutation - p.Tyr208Ser		BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation - Gly451Asp,PDGFRβ: Mutation (SNP) - p.Arg705Cys,ROS1: Mutation (SNP) - p.Thr2260Met,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,KMT2C: Mutation (SNP) - p.His906Tyr				
Hemangiosarcoma	Spleen, Liver	249	No	Trametinib, Rapamycin	yes	1	20	MYC: Overexpressed ,MEK1/2: . Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		ERCC1/2: . Underexpressed ,BRCA1/2: Underexpressed ,STAT1: Overexpressed ,RRM1/2: Overexpressed ,NR3C1: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a:	BRAF: Mutation (SNP) - p.Ile322Val				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed ,GLUT1: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed ,CCND1: Overexpressed					
hemangiosarcoma	Spleen	442		Trametinib, Rapamycin	no	0	254	MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	MGMT: Underexpressed ,ERCC1/2: Underexpressed ,STAT1: Overexpressed ,RRM1/2: Overexpressed ,PIK3CA: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,P53: Mutation - p.Cys228Arg,P53: Mutation - p.Val262Ile				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										,BCL-XL: Overexpressed ,AKT: Overexpressed					
Hemangiosarcoma	Free floating - caudal abdominal. Right hepatic liver mass.	391	No	Rapamycin, Imatinib		0	363								
Hemangiosarcoma	Free floating - caudal abdominal. Right hepatic liver mass.	391	No	Rapamycin, Imatinib	no	0	363	MYC: Overexpressed ,MEK1/2: : Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST		PGP: Underexpressed ,HIF1a: Overexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,AKT: Overexpressed	KMT2D: Mutation - p.Leu990Ser,CDKN2A: Mutation - p.Asn18Asp				
Hemangiosarcoma	right kidney	211	No	Rapamycin, Imatinib, Apoquel, Dasatinib,	yes	1	171	MYC: Overexpressed ,mTOR: Overexpressed - CST,MEK1/2:	SETD2: Mutation - p.Tyr1268Phe	STAT1: Overexpressed ,RAS/RAF: Overexpressed ,PTPN11:	ROS1: Mutation (SNP) - p.Ile133Val,JAK3: Mutation (SNP) - p.Ala220Thr,P53: Mutation - p.Tyr224del	1 Actionable Finding: SETD2 3 Addition	8 Actionable Findings: CDK4, JAK1, KDR,	1. Imatinib (KIT/KDR inhibitor) - 10 mg/kg/day PO 2. Palladia (KIT/KDR	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
				Trametinib				Overexpressed - CST,KIT. . Overexpressed ,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		Overexpressed ,PIK3CA: Overexpressed ,NR3C1: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,ERCC2: Overexpressed ,E2F1: Overexpressed ,COX2: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed		al Findings of Importance: P53, JAK3 (SNP), ROS (SNP)	KIT, MEK1/2, mTOR, MYC 14 Additional Findings of Importance: AKT, BCL-XL, COX2, E2F1, ERCC2, GLUT1, HIF1a, JAK2, MDM2, NR3C1, PIK3CA, PTPN1, RAS/RAF, STAT1	inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 5. Dasatinib (SRC inhibitor) 0.5-0.7 mg/kg/every other day PO 6. Apoquel (JAK inhibitor)- dose per label 7. Vorinostat (MYC inhibitor) - 45 mg/kg/eve	2. Mutation of well described tumor suppressor gene (P53). 3. Previously identified canine single nucleotide polymorphisms (SNPs).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														ry other day PO 8. Potential therapeutic benefit from NSAIDs or glucocorticoids. 9. Biomarkers associated with generalized chemoresistance including doxorubicin and platinum based agents. 10. Potential intracellular signaling including JAK/STAT, MAPK, and AKT/PI3K/mTOR pathways.	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	spleen	333	No	Trametinib, Rapamycin	no	0	61	MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,PTPN11: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,AKT: Overexpressed	P53: Mutation - p.Ala127Val,ATRX: Mutation - p.His2195Gln	1 Actionable Finding: PIK3CA 2 Additional Findings of Importance: ATRX, P53	4 Actionable Findings: JAK1, KDR, MEK1/2 11 Additional Findings of Importance: AKT, HIF1a, JAK2, PTPN11, RAS/RAF, STAT1, VEGF, ERCC1/2, MGMT	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR/VEGFR inhibitor) - 10 mg/kg/day PO 3. Apoquel (JAK1 inhibitor) - dose per label 4. Intracellular signaling via JAK/STAT pathway 5. Potential tumor sensitivity to DNA damaging agents, platinum based agents and/or alkylating	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Mutation of well described tumor suppressor gene (P53).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														agents. 6. Biomarker associated with generalized chemoresistance and a hypoxic tumor environment.	
Hemangiosarcoma	spleen	130	No	Trametinib, Rapamycin	no	0	106	MYC: Overexpressed ,MEK1/2 : . Overexpressed - CST,KIT : . Overexpressed ,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	TOP2A: Overexpressed ,RAS/RAF: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	P53: Mutation - p.Tyr152Cys,BRCA2: Mutation - p.Met959Ile,BRCA2: Mutation (SNP) - p.Asn2929Asp	1 Actionable Finding: PIK3CA 3 Additional Findings of Importance: BRCA2, BRCA2, P53	7 Actionable Findings: CDK4, JAK1, KDR, KIT, MEK1/2, MYC 7 Additional Findings of Importance: AKT, CCND1, GLUT1,	1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 3. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) -	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Mutation of well described tumor suppressor genes (P53, BRCA2)

Tumor type		
Tumor Location		
Total Survival time (in Days)		
Radiation		
Targeted Drugs		
Previous cancer therapy		
Traditional Therapy		
Total Days on Targeted		
Actionable RNA Alterations		
Potentially Clinically Significant Findings		
Other RNA Alterations		
Other Potentially Clinical Significant Findings		
DNA Sequencing Findings		
Gene Expression Findings	HIF1a, RAS/RAF, TOP2A	
RNA Therapeutic Indications	0.02 mg/kg/day PO 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Apoquel (JAK inhibitor) - dose per label 7. Potentital therapeutic sensitivity to anthracyclines. 8. Biomarkers associated with generalized chemo resistance and a hypoxic tumor environment.	
DNA Therapeutic Indications		

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Spleen, liver	215	No	Trametinib, Rapamycin	no	0	158	MEK1/2: Overexpressed - CST,KIT: . Overexpressed ,CDK4: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed ,RRM1/2: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed	TERT: Mutation - p.Gln1102_Gln1103fs,P53: Mutation - p.Cys226Tyr	2 Additional Findings of Importance: P53, TERT	3 Actionable Findings: CDK4, KIT, MEK1/2 9 Additional Finding of Importance: HIF1a, MDM2, RAS/RAF, RRM1/2, TOP2A, VEGF, ERCC1/2, MGMT, PGP	1. Imatinib (KIT inhibitor) - 10 mg/kg/day PO 2. Palladia (KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Potential tumor sensitivity to doxorubicin, platinum based and alkylating agents,	1. Mutation of well described tumor suppressor gene (P53). 2. Mutation of gene which encodes telomerase (TERT).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														especially associated with Rapamycin. 6. Suggestive tumor signaling via MAPK/ERK and/or AKT/PI3K intracellular pathways.	
Hemangiosarcoma	Right Atrium	76	No	Rapamycin, Imatinib, Apoquel	yes	1	31							1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Imatinib (KIT/KDR inhibitor) -	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO. 2. Mutation of well described tumor suppressor gene (P53). 3. Commonly altered
Hemangiosarcoma	Spleen	313	No	Imatinib, Rapamycin	yes	1	269	mTOR: Overexpressed - CST,MEK1/2: Overexpressed - CST,KIT. : Overexpressed ,KDR: Overexpressed - CST,JAK1: Overexpressed -	N-RAS: Mutation - p.Gln61Arg,BRAF: Mutation - p.Val105Leu	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,STAT1:	ROS1: Mutation (SNP) - p.Ile133Val,P53: Mutation - p.Asn143His,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FLT3: Mutation (SNP) - p.Thr142Ile	2 Actionable Findings: BRAF, N-RAS 4 Additional Findings of Importance: P53, FLT3,	6 Actionable Findings: CDK4, JAK1, KDR, KIT, MEK1/2, mTOR 17 Additional Findings of		

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								CST,CDK4: Overexpressed		Overexpressed ,RRM1/2: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,CCND1: Overexpressed ,BCL-XL: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed		KMT2C, ROS1	Importance: AKT, BCL6, BCL-XL, CCND1, GLUT1, HIF1a, JAK2, MDM2, RAS/RAF, RRM1/2, STAT1, TOP2A, BRCA1/2, ERCC1/2, MGMT, PGP	10 mg/kg/day PO 4. Palladia (KIT/KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 5. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 6. Apoquel (JAK1 inhibitor) - dose per label 7. High expression of HI1a and MDM2 impacts on tumor chemotherapy resistance ,but ,doxorubicin could have a potential action due	gene family in human malignancies (KMT). 4. Mutation identified in the protein tyrosine kinase domain (FLT3). 5. Canine single nucleotide polymorphisms (SNPs).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														to high TOP2A and low PGP expression 8. Gemcitabine is contraindicated for this case 9. Suggestive tumor signaling via MAPK/ERK and/or AKT/PI3K intracellular pathways.	
Hemangiosarcoma	spleen	361	No	Vorinostat	yes	1	120	MYC: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,KDR: Overexpressed - CST	PIK3CA: Mutation - p.Thr1025Ala	PGP: Underexpressed ,MGMT: Underexpressed ,BRCA1/2: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpr	FLT3: Mutation (SNP) - p.Thr142Ile,ROS1: Mutation - p.Thr729Met	1 Actionable Finding s: PIK3CA 2 Additional Finding of Importance: ROS1, FLT3	4 Actionable Findings: KDR, JAK1, MEK1/2, MYC 13 Additional Findings of	1. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Apoquel (JAK	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO. 2. Tyrosine kinase insulin receptor genes (ROS1). 3. Canine

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										essed ,RAS/RAF: Overexpressed ,PDGF: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,BCL-XL: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed			Importance: AKT, BCL6, BCL-XL, GLUT1, HIF1a, JAK2, RAS/RAF, PDGF, VEGF, ERCC1, BRCA 1/2, MGMT, PGP	inhibitor) - dose per label 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Potential tumor sensitivity to alkylating agents and platin-based chemotherapy. 6. Biomarkers associated with generalized chemoresistance.	single nucleotide polymorphism (SNP).
Hemangiosarcoma	Perineum (SQ)	522	No		no	0		MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,CD	PDGFRβ: Mutation (SNP) - p.Glu400Lys,mTOR: Mutation - p.Asp1376Glu	ERCC1/2: Underexpressed ,HIF1a: Overexpressed ,GLUT1:	KMT2C: Mutation (SNP) - p.His906Tyr,VEGFβ: Mutation (SNP) - p.Thr195Ala,VEGFβ: Mutation (SNP) - Intron variant,KMT2D: Mutation - p.Arg3083His,ABL1: Mutation - p.Val130Ile,ALK: Mutation - p.Leu104Val	"2 Actionable Findings: MTOR, PDGFRβ	3 Actionable Findings: CDK4, JAK1, MEK1/	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2.	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								K4: Overexpressed		Overexpressed ,AKT: Overexpressed		6 Additional Findings of Importance: ALK, ABL1, KMT2D, VEGFB (2), KMT2C	2 4 Additional Findings of Importance: AKT, GLUT1, HIF1a, ERCC 1/2	Apoquel (JAK inhibitor) - dose per label 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Potential tumor sensitivity to platin-based and alkylating therapy 5. Biomarkers associated with generalized chemo and radiation resistance.	2. Imatinib (PDGFR β inhibitor) - 10 mg/kg/day PO 3. Commonly altered gene family in human malignancies (KMT). 4. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	regrowth left flank and regional lymph node	38	No	Rapamycin, Dasatinib, Imatinib	yes	1	36	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2	EGFR: Mutation - p.Gly466Ala	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/	P53: Mutation - p.Arg163Trp,BRCA2: Mutation (SNP) - p.Asn2929Asp	1 Actionable Finding s: EGFR	6 Actionable Findings: CDK4, JAK1,	1. Dasatinib (CDK4 inhibitor) - 0.5-07 mg/kg/every other	1. Lapatinib (EGFR inhibitor)- 5-10 mg/kg/day PO

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								. . Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,BCL-XL: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed		2 Additional Finding of Importance: BRCA2, P53	KDR, MEK1/2, MYC, PDGFR 12 Additional Finding of Importance: AKT, BCL-XL, BCL6, CND1, HIFa, MDM2, RAS/RAF, VEGF, BRCA 1/2, ERCC 1/2, MGMT, PGP	day PO 2. Imatinib (KDR/PDGFR inhibitor)- 10 mg/kg/day PO 3. Palladia (KDR/PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Apoquel (JAK1 inhibitor) - dose per label 7. Potential	2. Mutation of well described tumor suppressor genes (P53, BRCA2)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														sensitivity to platin based and alkylating agents.	
Hemangiosarcoma	Mesentary	68	No		yes	1		MYC: Overexpressed ,MEK1/2: . Overexpressed - CST,KDR: Overexpressed - CST		ERCC1/2: . Underexpressed ,TOP2A: Overexpressed ,HIF1a: Overexpressed ,BCL-XL: Overexpressed	IDH1: Mutation (SNP) - p.Gly175Ser,P53: Mutation - p.Arg203Leu,P53: Mutation - p.Gln133*	3 Additional Findings of Importance: P53(2), IDH1	3 Actionable Findings: KDR, MEK1/2, MYC 4 Additional Finding of Importance: BCL-XL, HIF1a, TOP2A, ERCC1/2	1. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Biomarkers associated with generalized chemoresistance. 5. Potential sensitivity to	1. Mutation of well described tumor suppressor gene P53. 2. Previously identified canine SNP.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														anthracyclines (TOP2A) may be observed.	
Hemangiosarcoma	spleen and prescapular region on left	320	No	Rapamycin, Dasatinib	no	0	280	MET: Overexpressed ,MEK2: Overexpressed ,JAK1: Overexpressed - CST,CDK4: Overexpressed		RRM1/2: Underexpressed ,ERCC1/2: Underexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed	P53: Mutation - p.Arg327Cys,MET: Mutation (SNP) - p.Asp583Asn,BRCA2: Mutation - p.Leu2149Phe	3 Additional Finding of Importance: BRCA2, MET, P53	4 Actionable Findings: CDK4, JAK1, MEK2, MET 4 Additional Finding of Importance: HIF1a, JAK2, ERCC1/2, RRM1/2	1. Dasatinib (CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Crizotinib (MET inhibitor) - 1-2 mg/kg/day PO 4. Apoquel (JAK inhibitor) - dose per label 5. Potential tumor sensitivity to platin based	1. Mutation of well described tumor suppressor gene (BRCA2). 2. Mutation of well described tumor suppressor gene P53. 3. Canine single nucleotide polymorphism (SNP) (MET)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														agents and gemcitabine.	
Hemangiosarcoma	Spleen	142	No	Rapamycin, Trametinib, Dasatinib	yes	1	79	MEK1/2: Overexpressed - CST,KIT: Overexpressed ,KDR: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Leu (Canine HSA and Human Hotspot)	MGMT: Underexpressed ,PGP: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,HIF1a: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,NOTCH1: Mutation - p.Glu643Lys,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Gly59Ser,PDGFRβ: Mutation - p.Glu400Lys	1 Actionable Finding s: PIK3CA 4 Additional Findings of Importance: CREBBP, KMT2C, NOTCH1, PDGFRβ, ROS1	3 Actionable Findings: CDK4, KDR, KIT, MEK1/2 9 Additional Finding of Importance: AKT, CCND1, HIF1a, RRM2, TOP2A, BRCA1/2, ERCC1/2, PGP, MGMT	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 3. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Dasatinib (CDK4/SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Potential tumor sensitivity to anthracycl	1. Rapamycin (PIK3CA mutation) - 0.1 mg/kg/day PO 2. Mutated gene family commonly seen in human malignancies (KMT) 3. Canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														ines, alkylating agents, and platin based chemotherapy. 6. Potential tumor resistance to gemcitabine.	
Hemangiosarcoma	Spleen	385	No	Rapamycin, Imatinib	yes	1	3 1 4	MEK1/2: Overexpressed - CST,KIT. . Overexpressed ,KDR: Overexpressed - CST,CDK4: Overexpressed		MGMT: Underexpressed ,PGP: Underexpressed ,BRCA1/2: Underexpressed ,RRM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,ERCC1: Overexpressed ,COX2: Overexpressed	BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation - p.Gly264Asp	2 Additional Findings of Importance: BRCA1(2)	4 Actionable Findings: CDK4, KDR, KIT, MEK1/2 9 Additional Findings of Importance: AKT, COX2, ERCC1, GLUT1, HIF1a,	1. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Dasatinib (CDK4/SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK	1. Mutation of tumor suppressor gene (BRCA1). 2. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										,AKT: Overexpressed			RRM2. BRCA 1/2, PGP, MGMT	inhibitor) - 0.02 mg/kg/day PO 5. Potential tumor sensitivity to alkylating agents. 6. Potential tumor resistance to platin-based chemotherapies. 7. Potential resistance to gemcitabine. 8. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs).	
Hemangiosarcoma	Spleen	385	No	Rapamycin, Imatinib	yes	1	314	MEK1/2: Overexpressed - CST,KIT		MGMT: Underexpressed ,PGP:	BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation - p.Gly264Asp	2 Additional Finding	4 Actionable Findin	1. Imatinib (KDR/KIT inhibitor) - 10	1. Mutation of tumor suppress

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								. . Overexpressed ,KDR: Overexpressed - CST,CDK4: Overexpressed		Underexpressed ,BRCA1/2: Underexpressed ,RRM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,ERCC1: Overexpressed ,COX2: Overexpressed ,AKT: Overexpressed		s of Importance: BRCA1(2)	gs: CDK4, KDR, KIT, MEK1/2 9 Additional Findings of Importance: AKT, COX2, ERCC1, GLUT1, HIF1a, RRM2. BRCA 1/2, PGP, MGMT	mg/kg/day PO 2. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Dasatinib (CDK4/SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 5. Potential tumor sensitivity to alkylating agents. 6. Potential tumor resistance to platin-based chemothe	or gene (BRCA1). 2. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														rapies. 7. Potential resistance to gemcitabine. 8. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs).	
Hemangiosarcoma	spleen	197	No	Trametinib, Imatinib	yes	1	162	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST		ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,STAT1: Overexpressed ,HIF1a: Overexpressed ,BCL6: Overexpressed ,BCL-XL: Overexpressed ,AKT:	ROS1: Mutation (SNP) - p.Thr2260Met,BRAF: Mutation (SNP) - p.Ile322Val	2 Additional Findings of Importance: BRAF, ROS1	5 Actionable Findings: JAK1, KDR, MEK1/2, MYC, PDGFR 7 Additional Findings of Importance: AKT, BCL-	1. Imatinib (KDR/PDGFR inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR/PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO	1. Canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed			XL, BCL6, HIF1a, STAT1, BRCA 1/2, ERCC 1/2	4. Vorinostat (MYC inhibitor) - 30 mg/kg/every other day PO 5. Apoquel (JAK inhibitor) - dose per label 6. Potential sensitivity to platin based chemotherapy.	
Hemangiosarcoma	Subcutaneous	214	No	Trametinib, Vorinostat	yes	1	176	MEK2: Overexpressed ,KDR: Overexpressed - CST	ATM: Mutation - p.Ala989Val	MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,RAS/RAF: Overexpressed ,HIF1a: Overexpressed ,BCL-XL:	ROS1: Mutation (SNP) - p.Thr2260Met,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	1 Actionable Finding: ATM 2 Additional Findings of Importance: KMT2C, ROS1	2 Actionable Findings: KDR, MEK2 7 Additional Findings of Importance: AKT, BCL-XL,	1. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Mutated gene family commonly seen in human malignancies (KMT2C)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed ,AKT: Overexpressed			HIF1a, RAS/RAF, VEGF, ERCC 1/2, MGMT	mg/kg/day PO 4. Potential sensitivity to akylating and platin based chemotherapy	. 3. Canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	spleen	293	No		no	0		MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,CDK4: Overexpressed		PGP: Underexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,PIK3CA: Overexpressed ,HIF1a: Overexpressed ,ERCC2: Overexpressed ,CCND1: Overexpressed ,BCL-XL: Overexpressed ,AKT:	IDH1: Mutation (SNP) - p.Gly175Ser,BRCA1: Mutation (SNP) - p.Gly192Ser,BRAF: Mutation (SNP) - p.Ile322Val,P53: Mutation - p.Arg272His,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	5 Additional Findings of Importance: KMT2C, P53, BRAF, BRCA1, IDH1	3 Actionable Findings: CDK4, KDR, MEK1/2 8 Additional Findings of Importance: AKT, BCL-XL, CCND1, ERCC2, HIF1a, PIK3CA, RRM2,	1. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02 mg/kg/day	1. Mutated gene family commonly seen in human malignancies (KMT2C) 2. Mutation of well described tumor suppressor gene (P53) 3. Previously identified canine single nucleotide polymorp

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed			TOP2A, TYMS, PGP	PO 5. Potential tumor sensitivity to anthracyclines and/or 5-FU. 6. Potential tumor resistance to alkylating and/or platin based chemotherapy. 7. Potential tumor resistance to gemcitabine.	hism (SNP)
Hemangiosarcoma	Spleen (primary) Liver	120	No		no	0		MEK1/2: Overexpressed - CST,KIT. . Overexpressed ,KDR: Overexpressed - CST,JA		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,RRM2:	P53: Mutation (SNP) - p.Gly292Arg,ROS1: Mutation (SNP) - p.Arg1606His,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FGFR3: Mutation (SNP) - p.Arg146Trp	4 Additional Findings of Importance: FGFR3, KMT2C, ROS1, P53	4 Actionable Findings: JAK1, KDR, KIT, MEK1/2	1. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/eve	1. Polypeptide growth factor gene (FGFR3) 2. Mutated gene family

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								K1: Overexpressed - CST		Overexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed			8 Additional Findings of Importance: AKT, BCL-XL, GLUT1, HIF1a, RRM2, ERCC 1/2, MGMT, PGP	ry other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Apoquel (JAK1 inhibitor) - dose per label 5. Potential tumor sensitivity to alkylating agents and/or platin based chemotherapy. 6. Potential tumor resistance to gemcitabine.	commonly seen in human malignancies (KMT) 3. Previously identified canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	Rib, Spleen	110	No	Dasatinib	no	0	61	mTOR: Overexpressed - CST,MEK1/2:	SETD2: Mutation - Gly594Asp	MGMT: Underexpressed ,ERCC1/2:	ROS1: Mutation (SNP) - p.Arg1237Gln,JAK3: Mutation (SNP) - p.Gln305His,P53: Stop Gained - p.Tyr115*,KMT2D: Inframe Insertion - p.Lys2956_Gln2957insLysGln,KMT2C:	1 Actionable Finding: SETD2	5 Actionable Findings:	1. Dasatinib (CDK4 inhibitor) - 0.5-0.7	1. Vorinostat (HDAC inhibitor) - 30

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								Overexpressed - CST,KIT, . Overexpressed ,KDR: Overexpressed - CST,CDK4: Overexpressed		Underexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,RAS/RAF: Overexpressed ,PIK3CA: Overexpressed	Inframe Deletion - p.Gln1763del,ERBB2: Mutation - p.Leu43Val	6 Additional Findings of Importance: ERBB2, KMT2C, KMT2D, P53, JAK3, ROS1	CDK4, KDR, KIT, MEK1/2, mTOR 15 Additional Findings of Importance: AKT, CDKN2A, CCND1, E2F1, GLUT1, HIF1a, MDM2, NR3C1, PTEN, PIK3CA, RAS/RAF, TOP2A, TYMS, ERCC1/2, MGMT	mg/kg/every other day PO 2. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Imatinib (KDR/KIT inhibitor) - 10 mg/kg/day PO 5. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 6. Potential therapeutic benefit of glucocorticoids. 7. Biomarker	mg/kg/every other day PO 2. Tyrosine kinase receptor (ERBB2) 3. Mutated gene family commonly seen in human malignancies (KMT) 4. Mutation of well described tumor suppressor gene (P53) 5. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														s associated with generalized chemo-resistance. 8. Potential tumor sensitivity to alkylating and platinum based agents.	
Hemangiosarcoma	Splenic masses with suspect hepatic and mesenteric metastasis	136	No		no	0									
Hemangiosarcoma	Splenic masses with suspect hepatic and mesenteric metastasis	136	No		no	0		PDGFR: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JA	PIK3CA: Mutation - p.His1047Leu (Canine HSA and Human Hotspot)	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexp	CDKN2A: Mutation (SNP) - p.Ala89Ser,P53: Mutation - p.Phe260Ser,MIEN1: Mutation - p.Glu28_Tyr29fs,ATRX: Stop Gained - p.Glu2052*	1 Actionable Finding s: PIK3CA 4 Additional Findings of	5 Actionable Findings: CDK4, JAK1, KDR, MEK1/2, PDGFR	1. Imatinib (KDR/PDGFR inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR/PDGFR inhibitor) - 2.5-3.25	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Tumor suppressor gene in

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								K1: Overexpressed - CST,CDK4: Overexpressed		ressed ,VEGF: Overexpressed ,RAS/RAF: Overexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed		Importance: ATRX, MIEN1, P53, CDKN2A	10 Additional Findings of Importance: AKT, BCL6, HIF1a, PTEN, RAS/RAF, VEGF, ERCC 1/2, MGMT, PGP, RRM1/2	mg/kg/every other day PO 3. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 5. Apoquel (JAK1 inhibitor) - dose per label 6. Biomarkers of generalized chemo-resistance. 7. Potential tumor sensitivity to gemcitabine,	sarcomas (ATRX) 3. Membrane bound protein that modulates cell invasion (MIEN1) 4. Mutation of well described tumor suppressor gene (P53) 5. Canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														alkylating agents and/or platin based chemotherapy.	
Hemangiosarcoma	Spleen	148	Yes	Trametinib	yes	1	14	PDGFR: Overexpressed ,MEK1/2: . . Overexpressed - CST		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,RAS: Overexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed	CDKN2A: Mutation (SNP) - p.Ala89Ser	1 Additional Finding of Importance: CDKN2A	2 Actionable Findings: MEK1/2, PDGFR 10 Additional Findings of Importance: AKT, BCL-XL, HIF1a, PTEN, RAS, RRM2, TOP2A, ERCC1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (PDGFR inhibitor) - 10 mg/kg/day PO 3. Palladia (PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Potential tumor sensitivity to alkylating, platinum based agents and doxorubicin.	1. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														5. Potential tumor resistance to gemcitabine.	
Hemangiosarcoma	Spleen	164	No		no	0		MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	N-RAS: Mutation - p.Gln61Arg,NOTCH1: Mutation - p.Gly2179fs,MTOR: Mutation - p.Met1880Thr	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,TYMS: Overexpressed ,STAT1: Overexpressed ,RRM2: Overexpressed ,RAS/RAF: Overexpressed ,PTEN: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed	ROS1: Mutation (SNP) - p.Ile133Val,FLT3: Mutation (SNP) - p.Thr142Ile,KMT2D: Mutation - p.Pro1554Leu	3 Actionable Findings: mTOR, NOTCH1, NRAS 3 Additional Findings of Importance: KMT2D, FLT3, ROS1	4 Actionable Findings: CDK4, JAK1, KDR, MEK1/2 14 Additional Findings of Importance: AKT, BCL-XL, BCL6, JAK2, HIF1a, MDM2, PTEN, RAS/RAF, RRM2, STAT1, TYMS,	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Apoquel (JAK1	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 3. Vorinostat (MYC inhibitor) - 30 mg/kg/every other day PO 4. Commonly altered gene family in human malignancies (KMT)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										,HIF1a: Overexpressed ,BCL6: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed			ERCC 1/2, MGMT	inhibitor) - dose per label 6. Biomarkers of generalized chemo-resistance 7. Potential tumor sensitivity to 5-FU, alkylating agents and/or platin based chemotherapy. 8. Potential tumor resistance to gemcitabine.	5. Canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	Spleen	164	No		no	0		MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed -	N-RAS: Mutation - p.Gln61Arg,NOTCH1: Mutation - p.Gly2179fs,MTOR: Mutation - p.Met1880Thr	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,TYMS:	ROS1: Mutation (SNP) - p.Ile133Val,FLT3: Mutation (SNP) - p.Thr142Ile,KMT2D: Mutation - p.Pro1554Leu	3 Actionable Findings: mTOR, NOTCH1, NRAS 3	4 Actionable Findings: CDK4, JAK1, KDR, MEK1/2	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR inhibitor) - 10	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Trametinib (MEK

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								CST,CDK4: Overexpressed		Overexpressed ,STAT1: Overexpressed ,RRM2: Overexpressed ,RAS/RAF: Overexpressed ,PTEN: Overexpressed ,MDM2: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,BCL6: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed		Additional Findings of Importance: KMT2D, FLT3, ROS1	14 Additional Findings of Importance: AKT, BCL-XL, BCL6, JAK2, HIF1a, MDM2, PTEN, RAS/RAF, RRM2, STAT1, TYMS, ERCC 1/2, MGMT	mg/kg/day PO 3. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Apoquel (JAK1 inhibitor) - dose per label 6. Biomarkers of generalized chemo-resistance 7. Potential tumor sensitivity to 5-FU, alkylating agents and/or platin	inhibitor) - 0.02 mg/kg/day PO 3. Vorinostat (MYC inhibitor) - 30 mg/kg/every other day PO 4. Commonly altered gene family in human malignancies (KMT) 5. Canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														based chemotherapy. 8. Potential tumor resistance to gemcitabine.	
Hemangiosarcoma	Spleen (removed) and Liver	62	No	Trametinib, Rapamycin	no	0	34	MYC: Overexpressed ,MET: Overexpressed ,MEK2: Overexpressed ,KDR: Overexpressed - CST,EGFR: Overexpressed - CST		MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,PTEN: Overexpressed ,NR3C1: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed	NF1: Mutation (SNP) - p.Pro2364Ser,JAK2: Mutation (SNP) - p.Thr514Asn,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation (SNP) - p.Ala1873Thr,BRCA1: Mutation - p.Cys887Arg,BRCA1: Mutation - p.Val1230Ile,BRCA1: Mutation - p.Asp1431Glu	3 Additional Findings of Importance: BRCA1(5), JAK2, NF1	5 Actionable Findings: EGFR, KDR, MEK2, MET, MYC 12 Additional Findings of Importance: AKT, BCL6, COX2, HIF1a, MDM2, NR3C1, PTEN, RAS/RAF, STA1,	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 5. Crizotinib	1. Tumor suppressor gene (BRCA1) 2. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										,COX2: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed			VEGF, ERCC 1/2, MGMT	(MET inhibitor) - 1-2 mg/kg/day PO 6. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 7. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids. 8. Biomarkers associated with generalized chemoresistance. 9. Potential tumor sensitivity	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														to chemotherapy with alkylating and/or platinum based agents	
Hemangiosarcoma	Right flank	67	No	Trametinib, Rapamycin	no	0	39	MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - Gly106Val	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,TYMS: Overexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,COX2: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn	1 Actionable Finding s: PIK3CA 1 Additional Findings of Importance: MET	4 Actionable Findings: CDK4, JAK1, KDR, MEK1/2 10 Additional Findings of Importance: AKT, BCL6, COX2, HIF1a, PTEN, TYMS, ERCC 1/2, MGMT, PGP, RRM1/2	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Apoquel	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														(JAK1 inhibitor) - dose per label 6. Potential therapeutic benefit from NSAIDs 7. Biomarkers of generalized chemo-resistance 8. Potential tumor sensitivity to 5-FU, alkylating agents and/or platin based chemotherapy.	
Hemangiosarcoma	Subcutaneous, right medial distal tibia/tarsus region	100	No		unknown	0	30	MEK1/2: Overexpressed - CST,KIT. . Overexpressed ,KDR: Overexpressed - CST,JA	NOTCH1: Mutation - p.Asn2295fs,ATM: Mutation - p.Phe209fs	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2:	JAK2: Mutation - p.Pro841Arg	2 Actionable Findings: ATM, NOTCH1 1 Addition	5 Actionable Findings: CDK4, JAK1, KDR, KIT, MEK1/2	1. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 2. Imatinib (KDR/KIT inhibitor) - 10	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Potential protein

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								K1: Overexpressed - CST,CDK4: Overexpressed		Underexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,PTPN11: Overexpressed ,PTEN: Overexpressed ,MDM2: Overexpressed ,CDKN2A. . Overexpressed ,CCND1: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed		al Finding of Importance: JAK2	12 Additional Findings of Importance: AKT, BCL-XL, CCND1, CDKN2A, HIF1a, PTEN, PIK3CA, STAT1, ERCC 1/2, MGMT, PGP, RRM1/2	mg/kg/day PO 3. Palladia (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Apoquel (JAK inhibitor)- dose per label 6. Potential tumor sensitivity to gemcitabine as well as alkylating and and/or platinum based agents. 7. Potential	loss/loss of function (JAK2).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														intracellular signaling including JAK/STAT, MAPK, and AKT/PI3K pathways. 8. Biomarkers associated with radiation resistance.	
Hemangiosarcoma	Subcutaneous, right medial distal tibia/tarsus region	100	No	Trametinib	unknown	0	30								
Hemangiosarcoma	subcutaneous mass on back close to pelvic area	224	Yes		yes	1		MYC: Overexpressed ,MEK1/2: . Overexpressed - CST,KIT: . Overexpressed ,KDR: Overexpressed - CST,JA	SETD2: Mutation - Gly594Asp,SETD2: Mutation - p.Tyr1268Phe	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2:	KMT2C: Mutation (SNP) - p.His906Tyr,FLT3: Mutation - p.Val186Leu,ARID1A: Mutation (SNP) - Glu1377Gly,KMT2D: Mutation - p.Pro726Ser,CREBBP: Mutation - p.Gly1358Arg,BRCA2: Mutation (SNP) - p.Asn2929Asp	2 Actionable Findings: SETD2(2) 6 Additional Findings of Importance:	6 Actionable Findings: CDK4, JAK1, KDR, KIT, MEK1/2, MYC 8 Additio	1. Imatinib (KIT, KDR inhibitor) - 10 mg/kg/day PO 2. Palladia (KIT, KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametini	1. Vorinostat (HDAC) - 30 mg/kg/every other day PO 2. Tumor supressor gene (BRCA2) 3. Feature of malignan

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								K1: Overexpressed - CST,CDK4: Overexpressed		Underexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,AKT: Overexpressed		BRCA2, CREBBP, KMT2D, ARID1A ,FLT3, KMT2C	nal Findings of Importance: AKT, GLUT1, HIF1a, BRCA 1/2, ERCC 1/2, MGMT, PGP, RRM1/2	b (MEK inhibitor) - 0.02 mg/kg/day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Apoquel (JAK1 inhibitor) - dose per label 7. Biomarkers associated with generalized chemo-resistance 8. Potential tumor	t transformation (CREBBP) 4. Commonly altered gene family in human malignancies (KMT) 5. Canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														sensitivity to alkylating agents and/or platin based chemotherapy. 9, Potential tumor sensitivity to gemcitabine.	
Hemangiosarcoma	Spleen	203	No		yes	1	1 2	MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,RRM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,KMT2C: Mutation (SNP) - p.His906Tyr,P53: Mutation - p.Ser205Arg,ARID1A: Mutation - p.Ala822Thr	1 Actionable Finding s: PIK3CA 4 Additional Findings of Importance: ARID1A, P53, KMT2C, ROS1	4 Actionable Findings: CDK4, JAK1, KDR, MEK1/2 9 Additional Findings of Importance: AKT, BCL-XL, GLUT1,	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Member of the SWI/SNF family (ARID1A) 3. Mutation of well described tumor suppressor gene (P53) 4.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										,BCL-XL: Overexpressed ,AKT: Overexpressed			HIF1a, RRM2, BRCA 1/2, ERCC 1/2, MGMT, PGP	4. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 5. Apoquel (JAK inhibitor) - dose per label 6. Potential tumor sensitivity to alkylating and/or platinum based agents 7. Potential tumor resistance to gemcitabine	Previously identified canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	Retroperitoneum	168	No	Dasatinib, Vorinostat	yes	1	58	MYC: Overexpressed ,MEK1/2: : Overexpressed - CST,KDR: Overexp	ATM: Mutation - p.Pro2700Leu	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed	NOTCH1: Mutation (SNP) - p.Ser1456Asn,JAK2: Mutation (SNP) - p.Ile19Val	1 Actionable Finding s: ATM 2 Additional	5 Actionable Findings: CDK4, JAK1, KDR, MEK1/2,	1. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 2. Palladia (KDR inhibitor) - 2.5-3.25	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Previousl

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								ressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed		,BRCA1/2: Underexpressed ,VEGF: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,BCL6: Overexpressed ,AKT: Overexpressed		Findings of Importance: JAK2, NOTCH1	MYC 9 Additional Findings of Importance: AKT, BCL6, GLUT1, HIF1a, VEGF, BRCA 1/2, ERCC 1/2, MGMT, PGP	mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 6. Apoquel (JAK1 inhibitor) - dose per label 7. Biomarkers associated with generalize	y identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														d chemoresistance 8. Potential tumor sensitivity to alkylating agents and/or platin based chemotherapy.	
Hemangiosarcoma	abdominal mass	467	Yes		yes	1	1112	MEK1: Overexpressed ,KIT: Overexpressed ,KDR: Overexpressed - CST,JAK1: Overexpressed - CST	SETD2: Mutation - p.Tyr1268Phe	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn,P53: Mutation - p.Tyr115His,P53: Mutation - p.Lys109Arg,CREBBP: Mutation - p.Gly59Ser,BRCA2: Mutation - p.Pro3213Leu,CDK4: Mutation - p.Cys78Ser	2 Actionable Findings: CDK4, SETD2 5 Additional Findings of Importance: BRCA2, CREBBP, P53(2), MET	4 Actionable Findings: JAK1, KDR, KIT, MEK1 6 Additional Findings of Importance: HIF1a, PTEN, BRCA 1/2, ERCC 1/2,	1. Toceranib (KIT/KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KIT/KDR inhibitor) - 10 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Apoquel (JAK	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Tumor suppressor gene (BRCA2) 4. Feature of

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
													MGMT, PGP	inhibitor) - dose per label 5. Potential tumor sensitivity to alkylating agents and/or platin based chemotherapy.	malignant transformation (CREBBP) 5. Mutation of well described tumor suppressor gene (P53) 6. Previously identified canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	Right kidney region	48	No		unknown	0		MYC: Overexpressed ,MEK1: Overexpressed ,KDR: Overexpressed - CST,CDK4: Overexpressed		RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,BRCA1/2: Underexpressed ,PTEN:	MET: Mutation (SNP) - p.Asp583Asn,P53: Mutation - p.Ala77fs,KMT2D: Mutation - p.Leu990Ser,KMT2C: Mutation - p.Ser2135Asn	4 Additional Findings of Importance: KMT2C, KMT2D, P53, MET	4 Actionable Findings: CDK4, KDR, MEK1, MYC 10 Additional Findin	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day	1. Commonly altered gene family in human malignancies (KMT) 2. Mutation of well described tumor

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed ,HIF1a: Overexpressed ,COX2: Overexpressed ,CDKN2A . . Overexpressed ,AKT: Overexpressed			gs of Importance: AKT, CDKN2A, COX2, HIF1a, PTEN, BRCA 1/2, ERCC 1/2, MGMT, PGP, RRM1/2	PO 3. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 7. Potential tumor sensitivity to	suppressor gene (P53) 3. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														gemcitabine, alkylating and/or platin based chemotherapy.	
Hemangiosarcoma	mestastisis to the omentum and spleen	253	No	Trametinib, Rapamycin	yes	1	21 3	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	mTOR: Mutation - p.Asp1376Glu,N-RAS: Mutation - p.Gln61Arg	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,PIK3CA: Overexpressed	NF1: Mutation (SNP) - p.Ala1467Pro,MET: Mutation (SNP) - p.Asp583Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser,BRCA1: Mutation (SNP) - p.Gly192Ser,PDGFRβ: Mutation - p.Glu400Lys,BRCA1: Mutation - p.Val1230Ile,BRCA1: Mutation - p.Lys42Gln	2 Actionable Findings: N-RAS, mTOR 7 Additional Findings of Importance: BRCA1(3), CDKN2A, NF1, MET, PDGFRβ	6 Actionable Findings: CDK4, JAK1, KDR, MEK1/2, MYC, PDGFR 16 Additional Findings of Importance: AKT, BCL6, COX2, HIF1a, JAK2, MDM2, NR3C1, PTEN, PIK3C	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5.	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 3. Tumor suppressor gene (BRCA1) 4. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
													A, RAS/RAF, STAT1, TOP2A, VEGF, ERCC 1/2, MGMT, PGP	Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Apoquel (JAK inhibitor) - dose per label 7. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids 8. Biomarkers associated with generalized chemo-resistance 9. Potential tumor sensitivity to	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														alkylating agents 10. Potential resistance to doxorubicin that may be re-sensitized with Rapamycin 11. Platinum-drug resistance biomarker is expressed in this tumor (MDM2)	
Hemangiosarcoma	splenic HSA with liver met and omental metastases. Chest metastases on films and CT scan. Possible spread to nasal cavity and brain.	581	No	Rapamycin, Vorinostat, Trametinib, Toceranib	yes	1	207	MYC: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,CDK4: Overexpressed		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,VEGF: Overexpr	ROS1: Mutation (SNP) - p.Thr2260Met,RET: Mutation - p.Glu246Val,P53: Mutation - p.Arg145His,BRCA2: Mutation (SNP) - p.Asn2929Asp	4 Additional Findings of Importance: BRCA2, P53, RET, ROS1	5 Actionable Findings: CDK4, KDR, MEK1/2, MYC 13 Additional Findings of	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Trametini	1. Tumor supressor gene (BRCA2) 2. Mutation of well described tumor suppressor gene (P53) 3. Tyrosine kinase receptor

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										essed ,TYMS: Overexpressed ,RRM2: Overexpressed ,PTPN11: Overexpressed ,PTEN: Overexpressed ,PDGF: Overexpressed ,JAK1: Overexpressed - CST,HIF 1a: Overexpressed ,GLUT1: Overexpressed ,AKT: Overexpressed			Importance: AKT, GLUT1, HIF1a, JAK1, PDGF, PTEN, PTPN11, RRM2, TYMS, VEGF, BRCA 1/2, ERCC 1/2, MGMT, PGP	b (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Biomarkers associated with generalized chemo-resistance 7. Potential tumor resistance to gemcitabine 8. Potential	that activates multiple signal transduction pathways (RET) 4. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														tumor sensitivity to 5FU, alkylating agents and/or platin based agents	
Hemangiosarcoma	Primary Splenic with multifocal hepatic metastasis	63	No		no	0		MYC: Overexpressed ,MET: Overexpressed ,MEK2: Overexpressed ,KDR: Overexpressed - CST,JAK1: Overexpressed - CST		RRM1/2: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,STAT1: Overexpressed ,RAS/RAF: Overexpressed ,PTEN: Overexpressed ,PGP: Overexpressed ,MDM2: Overexpressed ,HIF1a:	P53: Mutation - p.Arg238Gln	1 Additional Findings of Importance: P53	5 Actionable Findings: JAK1, KDR, MEK2, MET, MYC 13 Additional Findings of Importance: AKT, BCL-XL, BCL6, COX2, DHFR, HIF1a, MDM2, PGP, RAS/RAF, PTEN,	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5.	1. Mutation of well described tumor suppressor gene (P53)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed ,DHFR: Overexpressed ,COX2: Overexpressed ,BCL6: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed			ERCC 1/2, MGMT , RRM1/2	Crizotinib (MET inhibitor) - 1-2 mg/kg/day PO 6. Apoquel (JAK inhibitor) - dose per label 7. Potential therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 8. Potential tumor sensitivity to gemcitabine and/or alkylating agents 9. Potential tumor resistance to doxorubicin that may be re-	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														sensitized with Rapamycin. 10. Platinum-drug resistance biomarker is expressed in this tumor (MDM2)	
Hemangiosarcoma	Spleen	270	No	Dasatinib, Rapamycin	no	0	173	SRC: Overexpressed - CST,PDGFR: Overexpressed ,MEK1/2. . Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	NOTCH1: Mutation - p.Arg277His,mTOR: Mutation - p.Asp1376Glu	MGMT: Underexpressed ,PGP: Underexpressed ,VEGF: Overexpressed ,TOP2A: Overexpressed	NOTCH1: Mutation (SNP) - p.Thr14Lys,SMARCA4: Mutation - p.Pro263_Gly264fs,RTP2: Mutation - p.Tyr215Ser,PDGFRα: Mutation - p.Arg696His,P53: Mutation - p.Leu103fs,KMT2D: Mutation (SNP) - p.Arg904Pro,KMT2D: Mutation - p.Gly899Val,KMT2D: Mutation - p.Met872Leu,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,BRCA2: Mutation - p.Thr1910Ala,ATRX: Mutation - p.Thr763Ala,ATRX: Mutation - p.Glu873Lys	2 Actionable Findings: mTOR, NOTCH1 10 Additional Findings of Importance: ATRX(2), BRCA2, KMT2C, KMT2D, P53, PDGFRa, RTP2,	6 Actionable Findings: CDK4, JAK1, KDR, MEK1/2, PDGFR, SRC 13 Additional Findings of Importance: AKT, BCL-XL, CCND	1. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Imatinib (KDR/PDGFR inhibitor) - 10 mg/kg/day PO 3. Toceranib (KDR/PDGFR inhibitor) - 2.5-3.25 mg/kg/every other day PO	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Tumor suppressor gene in sarcoma (ATRX) 3. Tumor supressor gene

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
												SMARCA4, NOTCH1	1, ERCC1, HIF1a, JAK2, MDM2, RAS/RAF, RRM1/2, TOP2A, VEGF, PGP, MGMT	4. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 5. Apoquel (JAK inhibitor) - dose per label 6. Biomarkers associated with generalized chemo-resistance 7. Potential tumor resistance to gemcitabine and/or platin based chemotherapy. 8. Potential resistance to doxorubicin that may be re-	(BRCA2) 4. Commonly altered gene family in human malignancies (KMT) 5. Mutation of well described tumor suppressor gene P53 6. Platelet-derived growth factor receptor (PDGFR) 7. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														sensitized with Rapamycin. 9. Potential tumor sensitivity to alkylating agents.	
Hemangiosarcoma	Spleen & Liver	173	No	Rapamycin, Trametinib, Toceranib	no	0	140	MYC: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,JAK1: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,VEGF: Overexpressed ,PTEN: Overexpressed ,JAK2: Overexpressed ,AKT: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn,P53: Mutation - p.Tyr150Ser,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,BRCA2: Mutation (SNP) - p.Pro2221Leu	1 Actionable Finding s: PIK3CA 4 Additional Findings of Importance: BRCA2, KMT2C, P53, MET	5 Actionable Findings: CDK4, JAK1, KDR, MEK1/2, MYC 7 Additional Findings of Importance: AKT, JAK2, PTEN, VEGF, ERCC 1/2, MGMT, PGP	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/eve	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Tumor supressor gene (BRCA2) 3. Commonly altered gene family in human malignancies (KMT) 4. Mutation of well described tumor suppressor gene

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	spleen	75	No	Trametinib, Toceranib, Rapamycin, Dasatinib, Apoquel	yes	1	47	MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot) ,MET: Mutation - p.Ile770Thr	RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2:	CDKN2A: Mutation (SNP) - p.Ala89Ser,P53: Mutation - p.Arg238Trp,PARP1: Mutation - p.Ser340Arg	2 Actionable Findings: MET, PIK3CA 3 Additional	3 Actionable Findings: CDK4, KDR, MEK1/2 11	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Toceranib (KDR inhibitor) -	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Crizotinib (MET
														ry other day PO 5. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 6. Apoquel (JAK inhibitor) - dose per label 7. Potential tumor sensitivity to alkylating agents and/or platin based chemotherapy	(P53) 5. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Underexpressed ,PTEN: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,HIF 1a: Overexpressed ,BCL6: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed		Findings of Importance: PARP1, P53, CDKN2A	Additional Findings of Importance: AKT, BCL-XL, BCL6, HIF1a, JAK1, JAK2, PTEN, ERCC 1/2, MGMT ,PGP, ,RRM1/2	2.5-3.25 mg/kg/every other day PO 3. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 4. Dasatinib (SRC/CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor sensitivity to gemcitabine, alkylating agents and/or platin	inhibitor) - 1-2 mg/kg/day PO 3. DNA damage repair gene (PARP1) 4. Mutation of well described tumor suppressor gene (P53) 5. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														based agents	
Hemangiosarcoma	spleen	206	No		yes	1	27	MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,CDK4: Overexpressed	N-RAS: Mutation - p.Gln61Arg	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,DHFR: Overexpressed ,BCL6: Overexpressed ,BCL-XL: Overexpressed ,AKT:	MET: Mutation (SNP) - p.Asp583Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser,BRCA1: Mutation - p.Thr1864Ile	1 Actionable Finding s: N-RAS 3 Additional Findings of Importance: BRCA1, CDKN2A, MET	3 Actionable Findings: CDK4, KDR, MEK1/2 12 Additional Findings of Importance: AKT, BCL-XL, BCL6, DHFR, HIF1a, JAK1, RRM2, TOP2A, BRCA 1/2, ERCC 1/2, MGMT, PGP	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 4. Dasatinib (CDK4 inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Tumor supressor gene (BRCA1) 3. Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed				6. Potential tumor sensitivity to doxorubicin, alkylating agents and/or platin based agents 7. Potential tumor resistance to gemcitabine	
Hemangiosarcoma	Spleen	165	No	Imatinib, Rapamycin	yes	1	30	CDK4: Overexpressed ,KDR: Overexpressed - CST,MEK1/2: Overexpressed - CST	PIK3CA: Mutation - p.Gly1049Arg	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,AKT: Overexpressed ,GLUT1:	ROS1: Mutation (SNP) - p.Lys2Arg,PDGFRB: Mutation (SNP) - p.Arg705Cys,NOTCH1: Mutation (SNP) - p.Ser1456Asn,P53: Mutation - p.Leu334Arg,P53: Mutation - p.Tyr152Asn,BRCA2: Mutation (SNP) - p.Asn2929Asp	1 Actionable Finding s: PIK3CA 6 Additional Findings of Importance: BRCA2, P53(2), NOTCH1,	3 Actionable Findings: CDK4, KDR, MEK1/2 8 Additional Findings of Importance: AKT,	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Trametinib (MEK inhibitor) -	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Tumor suppressor gene (BRCA2) 3. Mutation of well described tumor suppress

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										Overexpressed ,HIF1a: Overexpressed ,JAK1: Overexpressed - CST		PDGFRβ, ROS1	GLUT1, HIF1a, JAK1, BRCA 1/2, ERCC 1/2, MGMT, PGP	0.02-0.03 mg/kg/day PO 4. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor sensitivity to alkylating agents and/or platin based agents	or gene (P53) 4. Previously identified canine single nucleotide polymorphism (SNP)
Hemangiosarcoma	Spleen	118	No	Toceranib	no	0	69	MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,KIT: .		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexp	ROS1: Mutation (SNP) - p.Arg1606His,PDGFRβ: Mutation (SNP) - p.Arg705Cys,NTRK3: Mutation (SNP) - p.Ser42Asn,P53: Mutation - p.Leu184Arg,P53: Mutation - p.Met3Ile	5 Additional Findings of Importance: P53(2), NTRK3,	4 Actionable Findings: CDK4, KIT, KDR, MEK1/	1. Toceranib (KDR/KIT inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib	1. Mutation of well described tumor suppressor gene (P53) 2.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								Overexpressed ,CDK4: Overexpressed		ressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,PDGF: Overexpressed ,HIF1a: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed		PDGFRβ, ROS1	2 9 Additional Findings of Importance: AKT, BCL-XL, HIF1a, PDGF, TOP2, BRCA 1/2, ERCC 1/2, MGMT, PGP	(KDR/KIT inhibitor) - 10 mg/kg/day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor sensitivity to doxorubicin, alkylating agents and/or platin	Previously identified canine single nucleotide polymorphism (SNP)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														based agents	
Hemangiosarcoma	spleen	169	No	Trametinib	yes	1	91	MYC: Overexpressed ,MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,CDK4: Overexpressed	N-RAS: Mutation - p.Gln61Arg	MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,TOP2A: Overexpressed ,PTPN11: Overexpressed ,PDGF: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed	MET: Mutation (SNP) - p.Asp583Asn,BRCA1: Mutation (SNP) - p.Gly192Ser,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FGFR1: Mutation - p.Arg822His,BRCA1: Mutation - p.Lys42Gln,BRCA1: Mutation - p.Lys1074Glu,BRCA1: Mutation - p.Val1230Ile	1 Actionable Finding s: N-RAS 7 Additional Findings of Importance: BRCA1(4), FGFR1, KMT2C, MET	4 Actionable Findings: CDK4, KDR, MEK1/2, MYC 11 Additional Findings of Importance: AKT, BCL-XL, GLUT1, HIF1a. JAK1, PDGF, PTPN11, TOP2A, BRCA 1/2, ERCC 1/2, MGMT	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Palladia (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 5. Biomarkers associated with generalized chemo-	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Tumor suppressor gene (BRCA1) 3. Fibroblast growth factor receptor (FGFR1) 4. Commonly altered gene family in human malignancies (KMT) 5. Previously identified canine single nucleotide polymorp

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														resistance 6. Potential tumor sensitivity to doxorubicin, alkylating agents and/or platin based agents	hism (SNP)
Hemangiosarcoma	Spleen	69	No	Trametinib	yes	1	7	MYC: Overexpressed ,MEK1/2: . . Overexpressed - CST,KDR: Overexpressed - CST		VEGF: Overexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,PTEN: Overexpressed ,RAS/RAF: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpr		Unfortunately, DNA sequencing failed for the given sample.	3 Actionable Findings: KDR, MEK1/2, MYC 12 Additional Findings of Importance: AKT, BCL-XL, BCL6, GLUT1, HIF1a, JAK1,	1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Biomarker	Unfortunately, DNA sequencing failed for the given sample.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										essed ,GLUT1: Overexpressed ,BCL6: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed			JAK2, RAS/RAF, PTEN, TOP2A, TYMS, VEGF	s associated with generalized chemo-resistance 5. Potential tumor sensitivity to 5FU and/or doxorubicin.	
Hemangiosarcoma	spleen	267	No		yes	1		MEK1/2: Overexpressed - CST,KDR: Overexpressed - CST,CDK4: Overexpressed		VEGF: Overexpressed ,TYMS: Overexpressed ,TOP2A: Overexpressed ,RRM2: Overexpressed ,PTEN: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed ,CDKN2A	ROS1: Mutation (SNP) - p.Arg1606His,KMT2D: Mutation (SNP) - p.Pro876Leu,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	3 Additional Findings of Importance: KMT2C, KMT2D, ROS1	3 Actionable Findings: CDK4, KDR, MEK1/2 10 Additional Findings of Importance: AKT, CDKN2A, COX2, GLUT1, HIF1A, PTEN,	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Potential	1. Commonly altered gene family in human malignancies (KMT) 2. Previously identified canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
										. . Overexpressed ,AKT: Overexpressed			RRM2, TOP2A, TYMS, VEGF	therapeutic benefit of non-steroidal anti-inflammatory drugs (NSAIDs) 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor resistance to gemcitabine 7. Potential tumor sensitivity to 5FU and/or doxorubicin.	
Hemangiosarcoma	Spleen	50	No		no	0		MYC: Overexpressed ,MEK1/2 . . Overexpressed - CST,KD	NOTCH1: Mutation - p.Leu329Pro	VEGF: Overexpressed ,TYMS: Overexpressed ,STAT1: Overexpr	PDGFRβ: Mutation (SNP) - p.Arg705Cys,NTRK3: Mutation (SNP) - p.Ser42Asn,NOTCH1: Mutation (SNP) - p.Ser1456Asn,FLT3: Mutation (SNP) - p.Thr142Ile,BRCA1: Mutation (SNP) - p.Ala1873Thr,BRCA1: Mutation (SNP) - p.Arg337Ser,BRCA1: Mutation (SNP) - p.Lys155Glu,P53: Mutation (SNP) -	1 Actionable Finding s: NOTCH 1	4 Actionable Findings: CDK4, KDR, MEK1/	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO	1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
								R: Overexpressed - CST,CDK4: Overexpressed		essed ,RRM2: Overexpressed ,PTEN: Overexpressed ,PDGF: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,HIF1a: Overexpressed ,GLUT1: Overexpressed ,AKT: Overexpressed	p.Arg261His,P53: Inframe Deletion - p.Pro209_Pro212del	9 Additional Findings of Importance: P53(2), BRCA1(3), FLT3, NTRK3, NOTCH1, PDGFRβ	2, MYC 10 Additional Findings of Importance: AKT, GLUT1, HIF1a, JAK1, JAK2, PDGF, PTEN, RRM2, STAT1, TYMS	2. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 5. Biomarkers associated with generalized chemo-resistance 6. Potential tumor resistance to gemcitabine 7.	2. Mutation of well described tumor suppressor gene (P53) 3. Previously identified canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														Potential tumor sensitivity to 5FU and/or methotrexate.	
Hemangiosarcoma	Spleen	192	No		yes	1						No individualized gene mutations were identified.			
Hemangiosarcoma	Spleen	136	No	Vorinostat	yes	1	11		SETD2: Mutation - p.Pro5Gln		ROS1: Mutation (SNP) - p.Thr2260Met,PDGFRβ: Mutation (SNP) - p.Arg705Cys,NTRK3: Mutation (SNP) - p.Ser42Asn,RET: Mutation - p.Ala975Val,P53: Mutation - p.Met227Lys	1 Actionable Findings: SETD2 5 Additional Findings of Importance: P53, RET, NTRK3, PDGFRβ, ROS1		1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4.	1. Vorinostat (HDAC inhibitor)- 30 mg/kg/every other day PO 2. Mutation of well described tumor suppressor gene (P53) 3. Tyrosine kinase receptor (RET) 4. Canine single nucleotid

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO	e polymorphism (SNP).
Hemangiosarcoma	spleen	172	No		yes	1	32		PTEN: Mutation - p.Arg108Gln		ROS1: Mutation (SNP) - p.Thr2260Met,FLT3: Mutation (SNP) - p.Thr142Ile,RET: Mutation - p.Ala975Val,P53: Mutation - p.Ser175fs,FGFR2IIC: Mutation - p.Thr368Met,ATRX: Mutation - p.Arg2108Gly,ALK: Stop Gained - p.Gly1616*	1 Actionable Findings: PTEN 7 Additional Findings of Importance: ALK, ATRX, FGFR2IIC, P53, RET, FLT3, ROS1		1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Tyrosine kinase receptors (ALK, RET) 3. Tumor suppressor gene in sarcomas and other malignancies (ATRX) 4. Fibroblast growth factor receptor (FGFR2IIC) 5.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															Mutation of well described tumor suppressor gene (P53) 6. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	spleen	172	No	Dasatinib, Rapamycin	yes	1	32		PTEN: Mutation - p.Arg108Gln		ROS1: Mutation (SNP) - p.Thr2260Met,FLT3: Mutation (SNP) - p.Thr142Ile,RET: Mutation - p.Ala975Val,P53: Mutation - p.Ser175fs,FGFR2IIIC: Mutation - p.Thr368Met,ATRX: Mutation - p.Arg2108Gly,ALK: Stop Gained - p.Gly1616*	1 Actionable Finding s: PTEN 7 Additional Findings of Importance: ALK, ATRX, FGFR2IIIC, P53, RET, FLT3, ROS1		1. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 2. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 4. Vorinostat	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Tyrosine kinase receptors (ALK, RET) 3. Tumor suppressor gene in sarcomas and other malignancies (ATRX) 4.

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
														(HDAC inhibitor) - 30 mg/kg/every other day PO	Fibroblast growth factor receptor (FGFR2IIIC) 5. Mutation of well described tumor suppressor gene (P53) 6. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	Spleen, pulmonary, omentum	146	No	Rapamycin, Dasatinib	yes	1	62								
Hemangiosarcoma	Spleen	194	No	Toceranib, Dasatinib, Rapamycin	no	0	181		RET: Mutation - p.Ala975Val		ROS1: Mutation (SNP) - p.Ile133Val,NOTCH1: Mutation (SNP) - p.Ala2121Thr,P53: Mutation - p.Ser229Phe	1 Actionable Finding: RET 3 Additional Findings of Importance: P53,			1. Toceranib (RTK inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Mutation of well described tumor suppress

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
												NOTCH 1, ROS1			or gene (P53). 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	Spleen	148	No	Dasatinib, Rapamycin	no	0	47								
Hemangiosarcoma	Spleen	148	No	Dasatinib, Rapamycin	no	0	47				ROS1: Mutation (SNP) - p.Arg1606His,KMT2C: Mutation - p.Arg4182His,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	3 Additional Findings: KMT2C(2), ROS1			1. Commonly altered gene family in human malignancies (KMT) 2. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Spleen & Liver	85	No	Trametinib, Rapamycin	no	0	51		PTEN: Mutation - p.Arg108Gln,NF1: Mutation (SNP) - p.Arg2561Gln,ATM: Mutation - p.Ala989Val		PDGFRβ: Mutation (SNP) - p.Arg705Cys,P53: Mutation - p.Arg327Cys	3 Actionable Findings: ATM, NF1, PTEN 2 Additional Findings: P53, PDGFRβ			1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 3. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 4. Mutation of well described tumor suppressor gene (P53) 5. Canine single nucleotide polymorphism (SNP).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Spleen	180	No	Rapamycin, Dasatinib	no	0	128		mTOR: Mutation - p.Asp1376Glu		PDGFRβ: Mutation (SNP) - p.Arg705Cys,JAK2: Mutation (SNP) - p.Thr514Asn,SMAD4: Mutation - p.Pro203Ser	1 Actionable Findings: mTOR 3 Additional Findings: SMAD4, JAK2, PDGFRβ			1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Tumor suppressor and transcription factor gene (SMAD4) 3. Previously identified canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	spleen	223	No	Dasatinib	yes	1	0				ROS1: Mutation (SNP) - p.Arg1237Gln,MET: Mutation (SNP) - p.Asp583Asn,CREBBP: Mutation (SNP) - p.Gly2097Ser,CDKN2A: Mutation (SNP) - p.Ala89Ser,ARID1A: Inframe Deletion - p.Gln483_Pro484del	5 Additional Findings: ARID1A, CDKN2A, CREBBP, MET, ROS1			1. Member of the SWI/SNF family (ARID1A) 2. Previously identified canine single nucleotid

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															e polymorphism (SNP).
Hemangiosarcoma	spleen	153	No	Vorinostat	yes	1	80		PIK3CA: Mutation - p.Gly1049Arg,ATM: Mutation - p.Ala989Val		IDH1: Mutation (SNP) - p.Gly175Ser,PDGFRα: Mutation - p.Arg696His,P53: Mutation - p.Arg239Gln,P53: Mutation - p.Asp60Gly	2 Actionable Finding s: ATM, PIK3CA 3 Additional Finding s: P53(2), PDGFRα, IDH1			1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Mutation of well described tumor suppressor gene (P53) 4. Tyrosin kinase receptor (PDGFRα) 5. Canine single nucleotide polymorp

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															hism (SNP).
Hemangiosarcoma	spleen	200	No	Trametinib	no	0	152		NOTCH1: Mutation - p.Arg468_Asp469fs,N-RAS: Mutation - p.Gln61Arg,ATM: Mutation - p.Ala989Val		CDK4: Mutation - p.Cys78Ser,BRCA2: Mutation - p.Val1042Ile	3 Actionable Finding s: ATM, N-RAS, NOTCH 1 2 Additional Finding s: BRCA2, CDK4			1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 3. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 4. Tumor supressor gene (BRCA2) 5. Cyclin dependent kinase protein that regulates cell cycle (CDK4).

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	LEFT UPPER CERVICAL REGION with possible metastases to the lungs	140	No	Rapamycin, Vorinostat	no	0	89				NTRK2: Mutation (SNP) - p.Leu112Met,MET: Mutation (SNP) - p.Asp583Asn,P53: Mutation - p.Gly269fs,KMT2D: Mutation - p.Leu990Ser,JAK2: Mutation - p.Arg303His,CREBBP: Mutation - p.Gly59Ser,BRCA2: Mutation (SNP) - p.Asn2929Asp	7 Additional Findings: BRCA2, CREBBP, JAK2, KMT2D, P53, MET, NTRK2			1. Tumor suppressor gene (BRCA2) 2. Feature of malignant transformation (CREBBP) 3. Tyrosine kinase involved in intracellular signal transduction (JAK2) 4. Commonly altered gene family in human malignancies (KMT) 5. Mutation of well described tumor suppressor gene

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															(P53) 6. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	spleen	183	No		yes	1					NTRK3: Mutation (SNP) - p.Ser42Asn,BRCA2: Mutation (SNP) - p.Pro2221Leu	2 Additional Findings: BRCA2, NTRK3			1. Tumor suppressor gene, potential sensitivity to platin based agents (BRCA2) 2. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	Spleen & Liver	79	No	Trametinib, Rapamycin	no	0	54		N-RAS: Mutation - p.Gln61Arg,ATM: Mutation - p.Ala1273Thr			2 Actionable Findings: ATM, N-RAS			1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Vorinostat (HDAC inhibitor)-30 mg/kg/every other

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															day PO 3. Potential sensitivity to DNA damaging agents (ATM).
Hemangiosarcoma	Spleen & Liver	79	No	Trametinib, Rapamycin	no	0	54		N-RAS: Mutation - p.Gln61Arg,ATM: Mutation - p.Ala1273Thr			2 Actionable Findings: ATM, N-RAS			1. Trametinib (MEK inhibitor) - 0.02-0.03 mg/kg/day PO 2. Vorinostat (HDAC inhibitor)-30 mg/kg/every other day PO 3. Potential sensitivity to DNA damaging agents (ATM).
Hemangiosarcoma	Spleen	133	No	Lapatinib	no	0	36		EGFR: Mutation (SNP) - p.Arg202Gln		VEGFC: Mutation - p.Val342Ile,MET: Mutation (SNP) - p.Asp583Asn,FLT3: Mutation - p.Val186Leu,ABL1: Mutation (SNP) - p.Ala925Thr,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FLT3: Mutation - p.Asp748Asn,CDK4: Mutation - p.Cys78Ser	1 Actionable Findings: EGFR 7			1. Lapatinib (EGFR inhibitor) - 5-10 mg/kg/day PO 2. Cyclin

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
												Additional Finding s: CDK4, FLT3(2) , KMT2C, ABL1, MET, VEGFC			dependent kinase protein that regulates cell cycle (CDK4) 3. Tyrosine kinase receptor (FLT3) - Toceranib can be considered 4. Commonly altered gene family in human malignancies (KMT) 5. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	Spleen	179	No	Vorinostat	yes	1	126				NTRK3: Mutation (SNP) - p.Ser42Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser,P53: Mutation - p.Met234Lys,CDK4: Mutation - p.Cys78Ser	4 Additional Finding s: CDK4, P53,			1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
												CDKN2A, NTRK3			day PO 2. Cyclin dependent kinase protein that regulates cell cycle (CDK4) 3. Previously identified canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	spleen, liver	152	No	Vorinostat	yes	1	115		NOTCH1: Mutation (SNP) - p.Val2035Ile		CDKN2A: Mutation (SNP) - p.Ala89Ser,ABL1: Mutation (SNP) - p.Leu830Phe,KMT2D: Mutation - p.Leu990Ser	1 Actionable Finding s: NOTCH 1 3 Additional Finding s: KMT2D, ABL1, CDKN2A			1. Vorinostat (HDAC inhibitor) - 30 mg/kg/every other day PO 2. Commonly altered gene family in human malignancies (KMT) 3. Canine single

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															nucleotide polymorphism (SNP).
Hemangiosarcoma	Spleen with liver metastasis	106	No	Lapatinib		0	76								
Hemangiosarcoma	Spleen with liver metastasis	106	No	Lapatinib	no	0	76		P53: Mutation - p.Arg238Trp,EGFR: Mutation - p.Ala386Pro		KMT2D: Mutation (SNP) - p.Pro876Leu,KMT2C: Mutation (SNP) - p.His906Tyr,ARID1A: Mutation - p.Lys1407fs	5 Mutations Identified: ARID1A, EGFR, KMT2C, KMT2D, P53 1 Mutations Indicating Potential Therapeutic Approaches: EGFR			POTENTIAL CLINICAL SIGNIFICANCE EGFR: Lapatinib (EGFR inhibitor). P53: Potential resistance to anthracyclines, alkylating, antimetabolites and platin based agents. Consider HDAC inhibitor. UNKOWN

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															CLINICAL SIGNIFICANCE ARID1A: Member of the SWI/SNF family KMT2C: Previous identified as a SNP in canine. KMT2D: Previous identified as a SNP in canine.
Hemangiosarcoma	Spleen	82	No		yes	1			N-RAS: Mutation - p.Gln61Arg		ROS1: Mutation (SNP) - p.Thr2260Met				POTENTIAL CLINICAL SIGNIFICANCE N-RAS: Trametinib (MEK inhibitor) UNKOWN CLINICAL SIGNIFICANCE ROS1: Previous identified

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															as a SNP in canine.
Hemangiosarcoma	Heart	81	No		yes	1			PIK3CA: Mutation - p.Met1043Leu,PDGFRα: Mutation - p.Arg696His,P53: Mutation - p.Arg238Trp,NOTCH1: Mutation - p.Glu643Lys		NTRK3: Mutation (SNP) - p.Ser42Asn				
Hemangiosarcoma	Spleen	122	No	Trametinib, Toceranib	yes	1	69		PDGFRβ: Mutation (SNP) - p.Glu400Lys,PDGFRα: Mutation - p.Arg696His,P53: Mutation - p.Leu100fs,N-RAS: Mutation - p.Gln61Arg		IDH1: Mutation (SNP) - p.Gly175Ser,CDKN2A: Mutation (SNP) - p.Ala89Ser				POTENTIAL CLINICAL SIGNIFICANCE N-RAS: Trametinib (MEK inhibitor) P53: Tumor supressor gene. Consider HDAC inhibitor. PDGFRα: Mutation in protein tyrosine kinase domain. (novel). Consider tyrosine kinase inhibitor. PDGFRβ

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
															: . Receptor associated with cellular growth signaling. Consider tyrosine kinase inhibitor. UNKOWN CLINICAL SIGNIFICANCE CDKN2A: . Previous identified as a SNP in canine. IDH1: Previous identified as a SNP in canine.
Hemangiosarcoma	Spleen	125	No		yes	1			BRCA1: Mutation - p.Gly264Asp,BRCA1: Mutation - p.Val1230Ile		JAK2: Mutation (SNP) - p.Thr514Asn,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation (SNP) - p.Ala1873Thr				
Hemangiosarcoma	Spleen	52	No	Vorinostat	no	0	9				VEGFβ: Mutation - p.Trp117Gly,NOTCH1: Mutation (SNP) - p.Ser1456Asn,CDKN2A: Mutation (SNP) - p.Ala89Ser				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Spleen	212	No		yes	1			KDR: Inframe Deletion - p.Asn720_Leu721del		MET: Mutation (SNP) - p.Asp583Asn,ARID1A: Mutation - p.Arg1772Gln				
Hemangiosarcoma	Spleen	141	No	Rapamycin, Vorinostat	yes	1	65		P53: Mutation - p.Met225Ile		BRAF: Mutation (SNP) - p.Ile322Val				
Hemangiosarcoma	Spleen	101	No	Toceranib, Trametinib	yes	1	38		N-RAS: Mutation - p.Gln61Arg,FLT3: Mutation - p.Val186Leu,BRCA2: Mutation - p.Ser606Leu		PDGFRβ: Mutation (SNP) - p.Arg705Cys				
Hemangiosarcoma	Spleen	4506	No	Trametinib	yes	1	24		SETD2: Mutation - p.Tyr1268Phe,N-RAS: Mutation - p.Gly13Arg,BRCA2: Mutation (SNP) - p.Asn2929Asp		KMT2D: Mutation - p.Leu990Ser,CDKN2A: Mutation (SNP) - p.Ala89Ser				
Hemangiosarcoma	Spleen	86	No	Rapamycin, Trametinib	yes	1	67		N-RAS: Mutation - p.Gln61Arg		FLT3: Mutation (SNP) - p.Thr142Ile				
Hemangiosarcoma	Abdominal mass	1204	No	Crizotinib, Vorinostat	yes	1	33		P53: Mutation - p.Ser229Phe,P53: Mutation - p.Arg164His,MET: Mutation - p.Thr497Pro,BRCA2: Mutation - p.Met3332Lys		VEGFβ: Mutation (SNP) - p.Thr195Ala,VEGFβ: Mutation (SNP) - p.Leu146Val,ARID1A: Mutation - p.Ala822Thr				
Hemangiosarcoma	Spleen and Liver	58	No		yes	1			SETD2: Mutation - p.Pro5Gln,SETD2: Mutation - Cys1678Tyr,mTOR: Mutation - p.Asp1376Glu		VEGFC: Mutation - p.Val342Ile,NTRK3: Mutation (SNP) - p.Ser42Asn,MET: Mutation (SNP) - p.Asp583Asn,CDK4: Mutation - p.Cys78Ser				
Hemangiosarcoma	Spleen	48	No		yes	1			PDGFRβ: Mutation - p.Glu1060Asp		VEGFβ: Mutation (SNP) - p.Thr195Ala,VEGFβ: Mutation (SNP) -				

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Hemangiosarcoma	Liver with omental metastasis	84	No	Rapamycin	yes	1	9		PTEN: Inframe Deletion - p.Lys175_Met176del		ARID1A: Mutation - p.Ala822Thr				
Hemangiosarcoma	Spleen	169	Yes	Trametinib, Rapamycin	yes	1	32		N-RAS: Mutation - p.Gln61Lys		ROS1: Mutation (SNP) - p.Ile133Val,JAK1: Mutation - p.Arg826Cys				
Hemangiosarcoma	Spleen	59	No	Rapamycin	yes	1	0				KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FLT3: Mutation (SNP) - p.Thr142Ile,CDKN2A: Mutation - p.Gly85_Thr86fs				
Hemangiosarcoma	Spleen	40	No	Vorinostat		0	0		SETD2: Mutation - Gly594Asp,SETD2: Mutation - p.Tyr1268Phe		ROS1: Mutation (SNP) - p.Arg1237Gln,NOTCH1: Mutation (SNP) - p.Ala2121Thr,MET: Mutation (SNP) - p.Gly937Ser,JAK2: Mutation (SNP) - p.Ile19Val,FGFR3: Mutation (SNP) - p.Arg146Trp,CDK4: Mutation - p.Cys78Ser				
Hemangiosarcoma	Liver	341	No		yes	1			RET: Mutation - p.Ala975Val		VEGFB: Mutation (SNP) - p.Thr195Ala,VEGFB: Mutation (SNP) - p.Leu146Val,NTRK2: Mutation - p.Gly211Glu,FGFR2IIIC: Mutation - p.Thr368Met,BRCA1: Mutation (SNP) - p.Gly192Ser,BRCA1: Mutation (SNP) - p.Gly451Asp,BRCA1: Mutation (SNP) - p.Ala1873Thr,ATRX: Mutation - p.Pro524Ser				
Hemangiosarcoma	Spleen	86	No	Vorinostat	yes	1	5		SETD2: Stop Gained - p.Arg70*						

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Hemangiosarcoma	Spleen and right retroperitoneal	62	No		yes	1					PDGFRβ: Mutation (SNP) - p.Glu400Lys,MET: Mutation (SNP) - p.Asp583Asn				
Hemangiosarcoma	Liver and spleen	181	No	Imatinib, Rapamycin, Toceranib, Vorinostat	no	0	12 1	KDR: Overexpressed - CST		PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,TYMS: Overexpressed ,RRM2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,BCL-XL: Overexpressed	ROS1: Mutation (SNP) - p.Thr2260Met,MET: Mutation (SNP) - p.Asp583Asn,BRAF: Mutation (SNP) - p.Ile322Val,P53: Mutation - p.Asn237Thr,P53: Mutation - p.Arg99_Leu100fs,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,FLT1: Mutation - p.His888fs	7 Additional Finding of Importance: FLT1, KMT2C, P53(2), BRAF, MET, ROS1	1 Actionable Findings: KDR 8 Additional Findings of Importance: BCL-XL, GLUT1, HIF1a, RRM2, TYMS, ERCC 1/2, MGMT, PGP	1. Toceranib (KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 2. Imatinib (KDR inhibitor) - 10 mg/kg/day PO 3. Biomarkers associated with generalized chemo-resistance 4. Potential tumor sensitivity to 5'FU, alkylating and/or platin based chemotherapy. 5. Potential	1. Cell surface receptor (FLT1) 2. Commonly altered gene family in human malignancies (KMT) 3. Mutation of well described tumor suppressor gene P53. 4. Previously identified canine single nucleotide polymorphism (SNP)

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														tumor resistance to gemcitabine.	
Hemangiosarcoma	Left femur	33	No			0			SETD2: Stop Gained - p.Gln1270*,P53: Mutation - p.Arg163Trp,P53: Mutation - p.Arg145His,MET: Mutation - P.Asn938Lys		NF1: Mutation (SNP) - p.Arg2561Gln				
Hemangiosarcoma	spleen	119	No		yes	1		MYC: Overexpressed ,MEK1/2: . Overexpressed - CST,JAK1: Overexpressed - CST,KIT: . Overexpressed ,KDR: Overexpressed - CST,CDK4: Overexpressed	PIK3CA: Mutation - p.His1047Arg (Canine HSA and Human Hotspot)	TOP2A: Overexpressed ,JAK2: Overexpressed ,HIF1a: Overexpressed ,GLUT1: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	P53: Mutation - p.Pro209Leu,P53: Mutation - p.Arg164His	1 Actionable Finding: PIK3CA 2 Additional Findings of Importance: P53 (2)	7 Actionable Findings: CDK4, KDR, KIT, JAK1, MEK1/2, MYC 7 Additional Findings of Importance: AKT, CCND1, COX2, GLUT1,	1. Imatinib (KIT, KDR inhibitor) - 10 mg/kg/day PO 2. Palladia (KIT, KDR inhibitor) - 2.5-3.25 mg/kg/every other day PO 3. Dasatinib (SRC inhibitor) - 0.5-0.7 mg/kg/every other day PO 4. Trametinib (MEK inhibitor) - 0.02	1. Rapamycin (mTOR inhibitor) - 0.1 mg/kg/day PO 2. Mutation of well described tumor suppressor gene. Potentially associated with poor prognosis.

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													HIF1a, JAK2, TOP2A	mg/kg/day PO 5. Apoquel (JAK inhibitor) - dose per label 6. Vorinostat (HDAC inhibitor) - 45 mg/kg/every other day PO 7. Potential therapeutic benefit of NSAIDs. 8. Potential tumor sensitivity to anthracyclines. 9. Biomarkers associated with generalized chemoresistance.	

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	Skin		No		yes	1			SETD2: Mutation - p.Pro1914Leu,PIK3CA: Mutation - p.Ser405Phe,P53: Stop Gained - p.Arg184*,P53: Mutation - p.Pro210Gln,mTOR: Mutation - p.Asp1376Glu,MET: Mutation - p.Ser1328Phe,KIT: Mutation - p.Glu973Lys,FBXW7: Mutation - p.Arg440Gly,ERBB2: Mutation - p.Ser72Phe,BRCA2: Mutation - p.Leu605Phe,BRCA2: Mutation - p.Ser299Leu,BRCA1: Mutation - p.Pro789Ser,ATM: Stop Gained - p.Gln2988*,ATM: Mutation - p.Ala1392Val		VEGFA: Mutation - p.Ser423Leu,TERT: Mutation - p.Arg842Lys,BCL6: Mutation (SNP) - p.Arg160Cys,ROS1: Mutation - p.Arg1604Lys,ROS1: Mutation - p.Gly281Glu,PTPRT: Mutation - p.Ala663Val,PTPRD: Mutation - p.Glu1573Lys,PTPRD: Mutation - p.Arg845Cys,PTPRD: Mutation - p.Pro262Leu,PTPRD: Mutation - p.Phe74Leu,NTRK3: Mutation - Mutation - Glu480Lys,NRTK2: Mutation - p.Arg718Cys,NTRK2: Mutation - p.Ser249Phe,NTRK1: Mutation - p.Thr414_Pro415fs,NOTCH1: Mutation (SNP) - p.Ser1456Asn,KMT2D: Mutation - p.Pro2317Leu,KMT2D: Mutation - p.Pro2671Ser,KMT2D: Mutation - p.Ser3567Phe,KMT2C: Mutation - p.Arg3798Cys,KMT2C: Mutation - p.His2360Tyr,KMT2C: Mutation - p.Asp1321Tyr,JAK3: Mutation (SNP) - p.Asp130Asn,JAK3: Mutation - P.Pro396Ser,JAK1: Mutation - p.Leu158Phe,FGFR3: Mutation - p.Phe760Val,FGFR3: Mutation - p.Gly144Arg,CREBBP: Mutation - p.Gly59Ser,CREBBP: Mutation - p.Pro225Ser,BRAF: Mutation (SNP) - p.Ile322Val,ALK: Mutation - p.Glu931Gly,ALK: Mutation - p.Asp524Asn,ALK: Mutation - p.Leu232Phe,ALK: Mutation - p.Gly8Glu					
Hemangiosarcoma	Spleen, liver		No		yes	1									
Hemangiosarcoma	Spleen		No		unknown	0					FLT3: Mutation (SNP) - p.Thr142Ile,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	2 Findings of			1. Commonly altered

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
												Unknown Clinical Significance: KMT2C, FLT3			gene family in human malignancies (KMT) 2. Canine single nucleotide polymorphism (SNP).
Hemangiosarcoma	Scapular mass		No		unknown	0									
Hemangiosarcoma	Spleen		No		yes	1					NF1: Mutation (SNP) - p.Arg2561Gln,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys				
Hemangiosarcoma			No		yes	1					NTRK3: Mutation (SNP) - p.Ser42Asn				
Hemangiosarcoma	L cranial dorsal lateral abdominal wall		No	Vorinostat		0			P53: Inframe Deletion - p.Thr201_Ser205del		ROS1: Mutation (SNP) - p.Ile133Val,JAK2: Mutation (SNP) - p.Ile19Val,JAK2: Mutation (SNP) - p.Thr514Asn				
Hemangiosarcoma	Spleen		Yes		yes	1					VEGFβ: Mutation (SNP) - p.Leu146Val,PDGFRβ: Mutation (SNP) - p.Arg705Cys,NTRK3: Mutation (SNP) - p.Ser42Asn,EGFR: Mutation (SNP) - p.Arg202Gln				
Hemangiosarcoma	Spleen		No		yes	1			N-RAS: Mutation - p.Gln61Arg		NOTCH1: Mutation (SNP) - p.Ala2121Thr,MET: Mutation (SNP) - p.Asp583Asn,KMT2D: Stop Gained - p.Arg3030*				
Hemangiosarcoma	Retroperitoneal		No		no	0					VEGFβ: Mutation (SNP) - p.Leu146Val,VEGFβ: Mutation (SNP) - p.Thr195Ala,ROS1: Mutation (SNP) - p.Thr2260Met,PDGFRβ: Mutation				

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
											(SNP) - p.Arg705Cys,KMT2D: Mutation (SNP) - p.Arg904Pro,EGFR: Mutation (SNP) - p.Arg202Gln,CDKN2B: Mutation (SNP) - p.Ala83Gly,CDKN2B: Mutation (SNP) - p.Ala83Pro				
Hemangiosarcoma	Spleen		No		yes	1			PDGFRβ: Mutation - p.Glu1060Asp		PDGFRβ: Mutation (SNP) - p.Arg705Cys,NOTCH1: Mutation (SNP) - p.Val2035Ile,JAK2: Mutation (SNP) - p.Thr514Asn,BCL2: Mutation (SNP) - p.Arg64_Arg65fs				
Hemangiosarcoma	spleen		No		yes	1			P53: Mutation - p.Arg163Trp,PIK3CA: Mutation - p.Glu453Lys						
Hemangiosarcoma	Spleen		No		no	0					PDGFRβ: Mutation (SNP) - p.Arg705Cys,KMT2D: Inframe Insertion - p.Leu815_Ser816insLeuSerProArgProGluGluProCysLeu,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,KMT2C: Mutation (SNP) - p.His906Tyr,FLT3: Mutation (SNP) - p.Thr142Ile,CDKN2B: Mutation (SNP) - p.Ala83Gly,CDKN2B: Mutation (SNP) - p.Ala83Pro,ABL1: Mutation (SNP) - p.Leu830Phe				
Hemangiosarcoma	Spleen		No			0			N-RAS: Mutation - p.Gln61Arg		ROS1: Mutation (SNP) - p.Thr2260Met,KMT2D: Mutation - p.Leu990Ser, KMT2C: Mutation - p.Asp1321Tyr				
Hemangiosarcoma	Spleen		No		no	0					VEGFβ: Mutation (SNP) - p.Thr195Ala,VEGFβ: Mutation (SNP) - p.Leu146Val,JAK2: Mutation (SNP) - p.Thr514Asn,CREBBP: Mutation - p.Gly59Ser,BRCA2: Mutation (SNP) - p.Ile2226Met,BRCA2: Mutation (SNP) - p.Ile830Val,BRCA2: Mutation (SNP) - p.Asn669Asp				
Hemangiosarcoma	Spleen		No			0									

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy	Total Days on Targeted	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinical Significant Findings	DNA Sequencing Findings	Gene Expression Findings	RNA Therapeutic Indications	DNA Therapeutic Indications
Hemangiosarcoma	spleen		No			0									
Hemangiosarcoma	Spleen		No			0									
Hemangiosarcoma	Prostate, Spleen		No			0									
Hemangiosarcoma	Excised right kidney and mass. Right retroperitoneal region		No			0									

Table 26: Treatment of Apocrine gland anal sac adenocarcinomas (AGASACA)

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	Admera Data
Anal Sac Adenocarcinoma	Left anal sac, metastaic sacral lymph nodes	545	No	Lapatinib	yes	1					
Anal Sac Adenocarcinoma	Anal sac	158	Yes		yes	1				RTP2: Mutation (SNP) - p.His97Tyr,FLT3: Mutation - p.Thr153Ile,NOTCH1: Mutation (SNP) - p.Ser1456Asn,EGFR: Mutation (SNP) - p.Arg202Gln	- EGFR p.Arg226Gln; FLT3 p.Thr153Ile; RTP2 p.His97Tyr; NOTCH1 p.Ser1163Asn
Anal Sac Adenocarcinoma	Right Anal Gland, Regional Lymph Nodes (sacral, hypogastric)	619	Yes	Toceranib, Lapatinib	yes	1					
Anal Sac Adenocarcinoma	right anal sac	450	No	Lapatinib, Trametinib	yes	1	MEK2: Overexpressed ,ERBB2 (HER2/neu): Overexpressed		PGP: Underexpressed ,ERCC1/2: Underexpressed ,PTEN: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed	VEGFC: Mutation - p.Val342Ile,KMT2D: Mutation (SNP) - p.Pro876Leu,FLT3: Mutation (SNP) - p.Thr142Ile,BRCA1: Mutation (SNP) - p.Gly192Ser,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,BRCA1: Mutation - p.Gly264Asp,ATRX: Mutation - p.Glu873Lys,ALK: Mutation - p.Pro976Leu,ABL1: Mutation - p.Pro783fs	ABL1 p.Pro783fs, KMT2C p.Lys3163_Leu3164insAsnLys, VEGFC p.Val342Ile; ALK p.Pro976Leu,; FLT3 p.Thr153Ile, - KMT2D p.Pro876Leu;BRCA1 p.Gly240Ser, - BRCA1 p.Gly264Asp, ATRX p.Glu873Lys

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	Admera Data
Anal Sac Adenocarcinoma	Anal Sac Gland	317	No	Lapatinib, Trametinib, Apoquel	yes	1	MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,ERBB2 (HER2/neu): Overexpressed ,CDK4: Overexpressed		RRM1/2: Underexpressed ,PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed	KMT2D: Mutation - p.Pro1554Leu	KMT2D p.Pro1554Leu
Anal Sac Adenocarcinoma	liver, LN	901	Yes	Trametinib	yes	1				RTP2: Mutation (SNP) - p.His97Tyr,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Pro2046_Gln2047del,BRCA2: Mutation - p.Met3332_Lys3333insIleLys	KMT2C p.Lys3163_Leu3164insAsn BRCA2 p.Met3332_Lys3333insIleLys; RTP2 p.His97Tyr;; CREBBP p.Pro2112_Gln2113del
Anal Sac Adenocarcinoma	right anal gland	63	No	Piroxicam, Toceranib, Lapatinib, Rapamycin, Trametinib	yes	1		NOTCH1: Mutation - p. Val2035Leu		JAK2: Mutation (SNP) - p.Ile19Val,ROS1: Mutation (SNP) - p.Ile133Val,RTP2: Mutation (SNP) - p.His97Tyr,ARID1A: Mutation - p.Ala822Thr	ROS1 p.Ile133Val; JAK2 p.Ile19Val,; ARID1A p.Ala822Thr,; RTP2 p.His97Tyr, NOTCH1 p.Val1742Leu
Anal Sac Adenocarcinoma	Left Inguinal Lymphnode, Perivulvar, Now dorsal and left of bladder trigone and urethra area	2421	No	Rapamycin, Lapatinib, Imatinib	yes	1	PDGFR: Overexpressed ,MYC: Overexpressed ,MEK1/2: Overexpressed - CST,ERBB2 (HER2/neu): Overexpressed	SETD2: Mutation - p.Asn946Asp,NOTCH1: Mutation - p.Thr332Ile	PGP: Underexpressed ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,RRM2: Overexpressed ,RAS/RAF:	VEGFB: Mutation (SNP) - Intron variant,TERT: Mutation - p.Gln1102_Gln1103fs,SMARCA4: Mutation - p.Asp1183Asn,P53: Mutation - p.Asn143His,NTRK3: Mutation (SNP) - p.Ser42Asn,KMT2D: Mutation - p.Gln746Arg,KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys	VEGFB p.Leu146Val;TERT p.Gln1102_Gln1103fs,; SMARCA4 p.Asp1183Asn,; SETD2 p.Asn946Asp,; P53 p.Asn143His,; NTRK3 p.Ser19Asn,; NOTCH1 p.Thr332Ile,; KMT2D p.Gln746Arg,; KMT2C p.Lys3163_Leu3164insAsnLys

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	Admera Data
									Overexpressed ,MDM2: Overexpressed ,GLUT1: Overexpressed ,CCND1: Overexpressed ,AKT: Overexpressed		
Anal Sac Adenocarcinoma	Perianal, suspect caudal abdominal LN, suspect pulmonary nodules, suspect mass at L6-L7 invading spinal cord	502	Yes		yes	1	MYC: Overexpressed ,MEK1/2: Overexpressed - CST,JAK1: Overexpressed - CST,ERBB2 (HER2/neu): Overexpressed ,CDK4: Overexpressed		ERCC1/2: Underexpressed ,BRCA1/2: Underexpressed ,RAS/RAF: Overexpressed ,MDM2: Overexpressed ,HIF1a: Overexpressed ,COX2: Overexpressed ,CCND1: Overexpressed ,BCL-XL: Overexpressed ,AKT: Overexpressed	KMT2C: Inframe Insertion - p.Lys3163_Leu3164insAsnLys,CREBBP: Mutation - p.Gly59Ser,BRCA1: Mutation (SNP) - p.Gly192Ser	KMT2C p.Lys3163_Leu3164insAsnLys; CREBBP p.Gly59Ser; BRCA1 p.Gly240Ser, BRCA1 p.Gly264Asp
Anal Sac Adenocarcinoma	Left anal sac	1342	Yes	Lapatinib, Trametinib	yes	1					
Anal Sac Adenocarcinoma	Right perianal	65	No		no	0	MEK1/2: Overexpressed - CST,ERBB2	BRAF: Mutation - p.Val588Glu (Canine and human hotspot mutation)	RRM1/2: Underexpressed ,PGP: Underexpressed	NOTCH1: Mutation (SNP) - p.Thr14Lys,KMT2D: Mutation (SNP) - p.Leu662Pro,KMT2D: Mutation (SNP) - p.Val2946Leu,KMT2D: Mutation (SNP)	BRAF p.Ile322Val, BRAF p.Val588Glu; KMT2D p.Gln764Arg,; KMT2D p.Leu662Pro; KMT2D

Tumor type	Tumor Location	Total Survival time (in Days)	Radiation	Targeted Drugs	Previous cancer therapy	Traditional Therapy Refractory (yes=1, no =0)	Actionable RNA Alterations	Potentially Clinically Significant Findings	Other RNA Alterations	Other Potentially Clinically Significant Findings	Admera Data
Anal Sac Adenocarcinoma	Pulmonary metastatic disease	1867	Yes	Lapatinib, Trametinib, Rapamycin	yes	1					
Anal Sac Adenocarcinoma	Rectal	265	Yes	Lapatinib, Trametinib	yes	1					
							(HER2/neu): Overexpressed ,CDK4: Overexpressed		d ,MGMT: Underexpressed ,ERCC1/2: Underexpressed ,STAT1: Overexpressed ,PTEN: Overexpressed ,JAK2: Overexpressed ,JAK1: Overexpressed - CST,CCND1: Overexpressed ,AKT: Overexpressed	- p.Pro2768Ser,BRAF: Mutation (SNP) - p.Ile322Val,KMT2D: Mutation - p.Gln746Arg,KMT2D: Mutation - p.Gly4140Ser,KMT2D: Mutation - p.Gly5259Ser,IDH2: Mutation (SNP) - p.Ala378Pro	p.Val2946Leu,; KMT2D p.Pro2768Ser,; KMT2D p.Gly4140Ser; KMT2D p.Gly5259Ser; IDH2 p.Ala381Pro; NOTCH1 p.Thr14Lys

Table 27

Total Subjects on Therapy	Total Subjects with Reported Outcomes	Total Subjects with Reported Adverse Effects	Total % of Subjects with Reported Outcomes with Adverse Effects
542	**464**	**156**	**34%**

Drug Name	Subjects on Therapy*	Subjects with Reported Outcomes*	Subjects with Reported Adverse Effects**	% of Subjects with Reported Outcomes with Adverse Effects
Trametinib	275	244	59	24%
Imatinib	83	76	18	24%
Lapatinib	162	141	31	22%
Dasatinib	94	85	26	31%
Toceranib	61	58	19	33%
Rapamycin****	192	176	37	21%
Crizotinib	9	7	3	43%
Vorinostat	89	77	26	34%
				29%

*Subjects on combination therapies are counted more than once. They are counted for each particular drug

**In XXX% of reported AEs, subjects were on combination targeted therapies making it difficult to determine which single therapy caused the AE or if the AE was due to the combination. In these cases, the AE was counted for all drugs. It is also unknown what percentage of subjects were on additional chemotherapy in combination with targeted therapy.

***Totals are not a sum of all events but total number of subjects affected.

****In XXXX% of reported Rapamycin AEs, the therapy was used in combination with other targeted therapies

Table 28
Number and Type of Adverse Effects Reported

Trametinib	Diarrhea	Vomiting	Inappetence	Lethargy	Skin Lesions
Mild	6%	5%	14%	3%	0%
Moderate	5%	1%	0%	2%	2%
Severe	0%	0%	0%	0%	0%
Rapamycin	Other less common effects - Anemia, Hemorrhagic Gastroenteritis				
Mild	10%	4%	6%	4%	0%
Moderate	2%	1%	3%	2%	0%
Severe	0%	0%	0%	0%	0%
Lapatinib	Other less common effects: Anemia				
Mild	7%	8%	9%	5%	0%
Moderate	8%	6%	5%	1%	2%
Severe	0%	0%	0%	0%	0%
Dasatinib	Other less common effects: Progressive Liver Enzyme Elevations, Oral ulcer				
Mild	9%	7%	3%	4%	0%
Moderate	1%	0%	3%	1%	0%
Severe	1%	1%	0%	1%	0%
Imatinib	Other less common effects: Elevated Kidney Values				
Mild	10%	5%	6%	1%	0%
Moderate	16%	14%	5%	4%	0%
Severe	0%	0%	0%	0%	0%
Vorinostat	Other less common effects: Anemia, Increased Cardiac Toxicity				
Mild	7%	5%	5%	5%	0.8%
Moderate	4%	2%	6%	4%	1%
Severe	0%	0%	0%	0%	0%
Trametanib	Other less common effects: Anemia, hemorrhagic gastroenteritis, electrolyte changes				
Mild	21%	0%	13%	3%	0%
Moderate	3%	5%	8%	3%	0%
Severe	0%	0%	0%	0%	0%
Crizotinib					
Mild	0%	0%	6%	1%	0%
Moderate	0%	14%	5%	4%	0%

Severe	0%	0%	0%	0%	0%

CLAIMS

1. A method of treating a subject with a cancer, comprising:

treating the subject with a cancer harboring at least one mutation in ataxia-telangiectasia mutated (ATM) kinase in a biological sample derived from the cancer; and if there is at least one mutation in ATM kinase, administering to the subject a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor.

2. The method of claim 1, further comprising identifying or having identified the at least one mutation in ATM kinase.

3. The method of claim 1 or 2, wherein the HDAC inhibitor is selected from the group consisting of: romidepsin, belinostat, panobinostat, vorinostat, givinostat, entinostat, tacedinaline, and mocetinostat.

4. The method of any one of the above claims, further comprising administering an effective amount of a DNA damaging chemotherapeutic agent.

5. The method of claim 4 , wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

6. The method of claim 5, wherein the DNA-alkylating agent is selected from the group consisting of: a nitrosourea, a triazene and a platinum agent.

7. The method of claim 6, wherein the DNA-alkylating agent is a nitrosourea.

8. The method of claim 7, wherein the nitrosourea is lomustine.

9. The method of any one of the above claims, further comprising performing surgery on the subject.

10. The method of any one of the above claims, further comprising administering an effective amount of at least one additional anti-cancer therapeutic agent.

11. The method of any one of the above claims, further comprising administering to the subject ionizing radiation.

12. The method of any one of the above claims, wherein the cancer harbors more than one mutant allele of ATM kinase.

13. The method of any one of the above claims, wherein the biological sample is a nucleic acid sample.

14. The method of claim 13, wherein the biological sample is a purified nucleic acid sample.

15. The method of claim 14, wherein the sample is DNA.

16. The method of claim 14, wherein the sample is RNA.

17. The method of claim 12, wherein the identifying is performed by sequencing a nucleic acid sample.

18. The method of any one of the above claims, wherein the subject is a canine.

19. The method of any one of the above claims, wherein the cancer is selected from the group consisting of: solid tumor, lymphoma, cutaneous T-cell lymphoma, peripheral T-cell lymphoma, sarcoma, histiocytic sarcoma, multiple myeloma, hemangiosarcoma, lymphosarcoma, osteosarcoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer and thyroid cancer.

20. The method of any one of the above claims, wherein the cancer is histiocytic sarcoma.

21. A method of treating a subject with cancer, comprising having determined at least one mutation in ATM kinase; and

administering to the subject a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor.

22. The method of claim 21, wherein the HDAC inhibitor is vorinostat.

23. The method of claim 21, further comprising administering a DNA damaging chemotherapeutic agent.

24. The method of claim 23; wherein the DNA damaging chemotherapeutic agent is lomustine.

25. The method of any one of the above claims, wherein the at least one mutation in ATM kinase is selected from: a missense mutation, a splice site mutation and a frameshift variant.

26. The method of claim 25, wherein the at least one mutation in ATM kinase inhibits ATM kinase activity.

27. A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Rapamycin

28. The method of claim 27, wherein the Rapamycin is administered at a dose equal to or less than 1 mg/kg.

29. The method of claim 28, wherein the Rapamycin is administered at a dose of 0.05-0.1 mg/kg.

30. The method of any one of claims 27-29, wherein the pharmaceutical composition is administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly.

31. The method of any one of claims 27-30, wherein the Rapamycin is administered orally.

32. The method of any one of claims 27-31, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

33. The method of claim 32, wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent.

34. The method of claim 33, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

35. The method of claim 33, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

36. The method of claim 33 wherein the targeted anti-cancer agent is selected from the group consisting of Crizotinib, Dasatinib Erlotinib, Gefinitib, Imatinib, Lapatinib, Sorafenib, Trametinib, and Vorinostat.

37. The method of claim 36, wherein the targeted anti-cancer agent is Dasatinib.

38. The method of any one of claims 27-36, further comprising performing surgery on the subject.

39. The method of any one of claims 27-37, further comprising administering to the subject ionizing radiation.

40. The method of any one of claims 27-38, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras.

41. The method of any one of claims 27-39, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras.

42. The method of claim 41 wherein the biological sample is a nucleic acid sample.

43. The method of claim 42, wherein the biological sample is a purified nucleic acid sample.

44. The method of claim 43, wherein the sample is DNA.

45. The method of claim 43, wherein the sample is RNA.

46. The method of claim 41, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

47. The method of any one of claims 27-46, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer.

48. The method of claim 47, wherein the cancer is hemangiosarcoma.

49. A pharmaceutical composition formulated for oral administration, comprising Rapamycin, wherein the Rapamycin is present at a concentration of 0.001 mg/mL-10.0 mg/mL.

50. A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Dasatinib.

51. The method of claim 50, wherein the Dasatinib is administered at a dose equal to or less than 2 mg/kg.

52. The method of claim 51, wherein the Dasatinib is administered at a dose of 0.5-0.7 mg/kg.

53. The method of any one of claims 50-52, wherein the Dasatinib is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5th day, or weekly.

54. The method of any one of claims 50-53, wherein the Dasatinib is administered orally.

55. The method of any one of claims 50-54, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

56. The method of claim 55, wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent.

57. The method of claim 56, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

58. The method of claim 55, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

59. The method of claim 58, wherein the targeted anti-cancer agent is selected from the group consisting of Crizotinib, Erlotinib, Gefinitib, Imatinib, Lapatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat.

60. The method of claim 59, wherein the targeted anti-cancer agent is Rapamycin.

61. The method of any one of claims 50-60, further comprising performing surgery on the subject.

62. The method of any one of claims 50-61, further comprising administering to the subject ionizing radiation.

63. The method of any one of claims 50-62, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase.

64. The method of any one claims 50-63, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase.

65. The method of claim 64, wherein the biological sample is a nucleic acid sample.

66. The method of claim 65, wherein the biological sample is a purified nucleic acid sample.

67. The method of claim 66, wherein the sample is DNA.

68. The method of claim 66, wherein the sample is RNA.

69. The method of claim 64, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

70. The method of any one of claims 50-69, wherein the cancer is selected from the group consisting of solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer.

71. The method of claim 70, wherein the cancer is osteosarcoma.

72. A pharmaceutical composition formulated for oral administration, comprising Dasatinib, wherein the Dasatinib is present at a concentration of 0.001 mg/mL-10.0 mg/mL.

73. A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Lapatinib.

74. The method of claim 73, wherein the Lapatinib is administered at a dose equal to or less than 50 mg/kg.

75. The method of claim 74, wherein the Lapatinib is administered at a dose of 5 mg/kg - 10 mg/kg.

76. The method of any one claims 73-75, wherein the Lapatinib is administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly.

77. The method of any one of claims 73-76, wherein the Lapatinib is administered orally.

78. The method of any one of claims 73-77, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

79. The method of claim 78, wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent.

80. The method of claim 79, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

81. The method of claim 78, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

82. The method of claim 81, wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Imatinib, Dasatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat.

83. The method of claim 82, wherein the targeted anti-cancer agent is Trametinib.

84. The method of any one of claims 73-82, further comprising performing surgery on the subject.

85. The method of any one of claims 73-84, further comprising administering to the subject ionizing radiation.

86. The method of any one of the above claims, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of ERBB1 and ERBB2.

87. The method of any one of claims 73-86, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ERBB1 and ERBB2.

88. The method of claim 87, wherein the biological sample is a nucleic acid sample.

89. The method of claim 88, wherein the biological sample is a purified nucleic acid sample.

90. The method of claim 89, wherein the sample is DNA.

91. The method of claim 89, wherein the sample is RNA.

92. The method of claim 87, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

93. The method of any one of claims 73-92, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma.

94. The method of claim 93, wherein the cancer is transitional cell carcinoma.

95. A pharmaceutical composition formulated for oral administration, comprising

Lapatinib, wherein the Lapatinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL.

96. A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Trametinib.

97. The method of claim 96, wherein the Trametinib is administered at a dose equal to or less than 0.05 mg/kg/day.

98. The method of claim 97, wherein the Trametinib is administered at a dose of 0.02 mg/kg/day.

99. The method of any one of claims 96-98, wherein the Trametinib is administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly.

100. The method of any one of claims 96-99, wherein the Trametinib is administered orally.

101. The method of any one of claims 96-100, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

102. The method of claim 101, wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent.

103. The method of claim 102, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

104. The method of claim 101, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

105. The method of claim 104, wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Imatinib, Dasatinib, Rapamycin, Sorafenib, Lapatinib, and Vorinostat.

106. The method of claim 105, wherein the targeted anti-cancer agent is Rapamycin.

107. The method of claim 105, wherein the targeted anti-cancer agent is Dasatinib

108. The method of claim 105, wherein the targeted anti-cancer agent is Lapatinib.

109. The method of any one of claims 96-108, further comprising performing surgery on the subject

110. The method of any one of claims 96-109, further comprising administering to the subject ionizing radiation.

111. The method of any one of claims 96-110, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of MEK1 and MEK2.

112. The method of any one of claims 96-111, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of MEK1 and MEK2.

113. The method of claim 112, wherein the biological sample is a nucleic acid sample.

114. The method of claim 113, wherein the biological sample is a purified nucleic acid sample.

115. The method of claim 113, wherein the sample is DNA.

116. The method of claim 113, wherein the sample is RNA.

117. The method of claim 112, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

118. The method of any one of the above claims, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma).

119. The method of claim 118, wherein the cancer is transitional cell carcinoma.

120. A pharmaceutical composition formulated for oral administration, comprising

Trametinib, wherein the Trametinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL.

121. A method of treating a cancer in a canine subject, comprising administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Vorinostat.

122. The method of claim 121, wherein the Vorinostat is administered at a dose equal to or less than 100 mg/kg.

123. The method of claim 122, wherein the Vorinostat is administered at a dose of 30-60 mg/kg.

124. The method of any one claims 121-123, wherein the Vorinostat is administered at a frequency selected from the group consisting of: twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly.

125. The method of any one of claims 121-124, wherein the Vorinostat is administered orally.

126. The method of any one of claims 121-125, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

127. The method of claim 126, wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent.

128. The method of claim 127, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

129. The method of claim 126, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

130. The method of claim 129, wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Imatinib, Dasatinib, Rapamycin, Sorafenib, Lapatinib, and Trametinib.

131. The method of claim 130, wherein the targeted anti-cancer agent is Rapamycin.

132. The method of claim 130, wherein the targeted anti-cancer agent is Trametinib.

133. The method of claim 130, wherein the targeted anti-cancer agent is Lapatinib.

134. The method of any one of claims 121-133, further comprising performing surgery on the subject

135. The method of any one of claims 121-134, further comprising administering to the subject ionizing radiation.

136. The method of any one of claims 121-135, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1.

137. The method of any one of claims 121-136, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1.

138. The method of claim 137, wherein the biological sample is a nucleic acid sample.

139. The method of claim 138, wherein the biological sample is a purified nucleic acid sample.

140. The method of claim 139, wherein the sample is DNA.

141. The method of claim 139, wherein the sample is RNA.

142. The method of claim 137 wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

143. The method of any one of claims 121-143, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma).

144. The method of claim 143, wherein the cancer is hemangiosarcoma.

145. The method of claim 143, wherein the cancer is histiocytic sarcoma.

146. A pharmaceutical composition formulated for oral administration, comprising Vorinostat, wherein the Vorinostat is present within the composition at a concentration of 0.01 mg/mL -500.0 mg/mL.

147. A method of treating a cancer in a canine subject, comprising administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Imatinib.

148. The method of claim 147, wherein the Imatinib is administered at a dose equal to or less than 50 mg/kg.

149. The method of claim 148, wherein the Imatinib is administered at a dose of 10 mg/kg.

150. The method of any one of claims 147-149, wherein the Imatinib is administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly.

151. The method of any one of claims 147-150, wherein the Imatinib is administered orally.

152. The method of any one claims 147-151, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

153. The method of claim 152, wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent.

154. The method of claim 153, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

155. The method of claim 154, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

156. The method of claim 155, wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat.

157. The method of claim 156, wherein the targeted anti-cancer agent is Trametinib.

158. The method of claim 156, wherein the targeted anti-cancer agent is Rapamycin.

159. The method of any one of claims 147-158, further comprising performing surgery on the subject

160. The method of any one of claims 147-159, further comprising administering to the subject ionizing radiation.

161. The method of any one of claims 147-160, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, PDGFR, and C-KIT.

162. The method of any one of claims 147-161, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ABL, BCR-ABL, PDGFR, and C-KIT.

163. The method of claim 162, wherein the biological sample is a nucleic acid sample.

164. The method of claim 163, wherein the biological sample is a purified nucleic acid sample.

165. The method of claim 164, wherein the sample is DNA.

166. The method of claim 164, wherein the sample is RNA.

167. The method of claim 162, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

168. The method of any one of claims 147-167, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma.

169. The method of claim 168, wherein the cancer is hemangiosarcoma.

170. The method of claim 168, wherein the cancer is mast cell tumor.

171. A pharmaceutical composition formulated for oral administration, comprising

Imatinib, wherein the Imatinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL.

172. A method of treating a cancer in a canine subject, comprising administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Crizotinib.

173. The method of claim 172, wherein the Crizotinib is administered at a dose equal to or less than 10 mg/kg.

174. The method of claim 173, wherein the Crizotinib is administered at a dose of 1 mg/kg-2 mg/kg.

175. The method of any one of claims 172-174, wherein the Crizotinib is administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly.

176. The method of any one of claims 172-175, wherein the Crizotinib is administered orally.

177. The method of any one of claims 172-176, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

178. The method of claim 177, wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent.

179. The method of claim 178, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

180. The method of claim 177, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

181. The method of claim 180, wherein the targeted anti-cancer agent is selected from the group consisting of: Imatinib, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat.

182. The method of claim 181, wherein the targeted anti-cancer agent is Trametinib.

183. The method of claim 181, wherein the targeted anti-cancer agent is Imatinib.

184. The method of any one of claims 171-183, further comprising performing surgery on the subject.

185. The method of any one of the claims 171-184, further comprising administering to the subject ionizing radiation.

186. The method of any one of claims 171-185, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of ALK, c-MET and ROS1.

187. The method of any one of claims 171-186, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ALK, c-MET and ROS1.

188. The method of claim 187, wherein the biological sample is a nucleic acid sample.

189. The method of claim 188, wherein the biological sample is a purified nucleic acid sample.

190. The method of claim 189, wherein the sample is DNA.

191. The method of claim 189, wherein the sample is RNA.

192. The method of claim 187, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

193. The method of any one of claims 172-192, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma.

194. The method of claim 193, wherein the cancer is hemangiosarcoma.

195. The method of claim 193, wherein the cancer is osteosarcoma.

196. A pharmaceutical composition formulated for oral administration, comprising

Crizotinib, wherein the Crizotinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL.

197. A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Sorafenib.

198. The method of claim 197, wherein the Sorafenib is administered at a dose of less than 10 mg/kg.

199. The method of claim 198, wherein the Sorafenib is administered at a dose of 1 mg/kg – 3 mg/kg.

200. The method of any one claims 197-199, wherein the Sorafenib is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5^{th} day, or weekly.

201. The method of any one of claims 197-200, wherein the Sorafenib is administered orally.

202. The method of any one of claims 197-201, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent.

203. The method of claim 202, wherein the at least one additional cancer agent is a DNA damaging chemotherapeutic agent.

204. The method of claim 203, wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent.

205. The method of claim 202, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent.

206. The method of claim 205, wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Dasatinib Erlotinib, Gefinitib, Imatinib, Lapatinib, Rapamycin, Trametinib, and Vorinostat.

207. The method of claim 206, wherein the targeted anti-cancer agent is Imatinib.

208. The method of any one of claims 197-207, further comprising performing surgery on the subject.

209. The method of any one of claims 197-208, further comprising administering to the subject ionizing radiation.

210. The method of any one claims 197-209, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB.

211. The method of any one of claims 197-210, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB.

212. The method of claim 211, wherein the biological sample is a nucleic acid sample.

213. The method of claim 212, wherein the biological sample is a purified nucleic acid sample.

214. The method of claim 213, wherein the sample is DNA.

215. The method of claim 213, wherein the sample is RNA.

216. The method of claim 211, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

217. The method of any one of claims 197-216, wherein the canine cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer.

218. The method of claim 217, wherein the cancer is mast cell tumor.

219. The method of claim 217, wherein the cancer is osteosarcoma.

220. A pharmaceutical composition formulated for oral administration, comprising Sorafenib, wherein the Sorafenib is present at a concentration of 0.001 mg/mL- 100.0 mg/mL.

221. The method of any one of claims of 1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219, wherein the cancer harbors at least one mutation in at least one gene shown in Tables 1, 2 and 12-26.

222. The method of any one of claims 1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219, further comprising determining or having determined from a biological sample derived from the cancer, at least one mutation in at least one gene shown in Tables 1, 2, and 12-26.

223. The method of any one of claims 1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219, wherein the cancer has increased or decreased expression in at least one gene shown in Tables 1, 2 and 12-26 compared to non-cancerous tissue.

224. The method of any one of claims 1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219, further comprising determining or having determined from a biological sample derived from the cancer, increased or decreased expression in at least one gene shown in Tables 1, 2, and 12-26 compared to non-cancerous tissue.

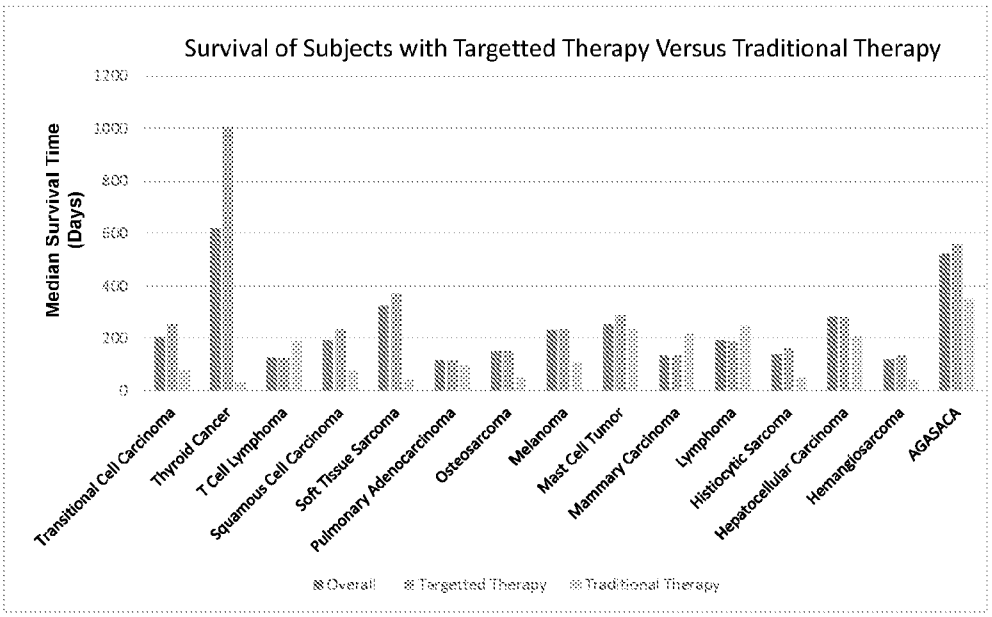
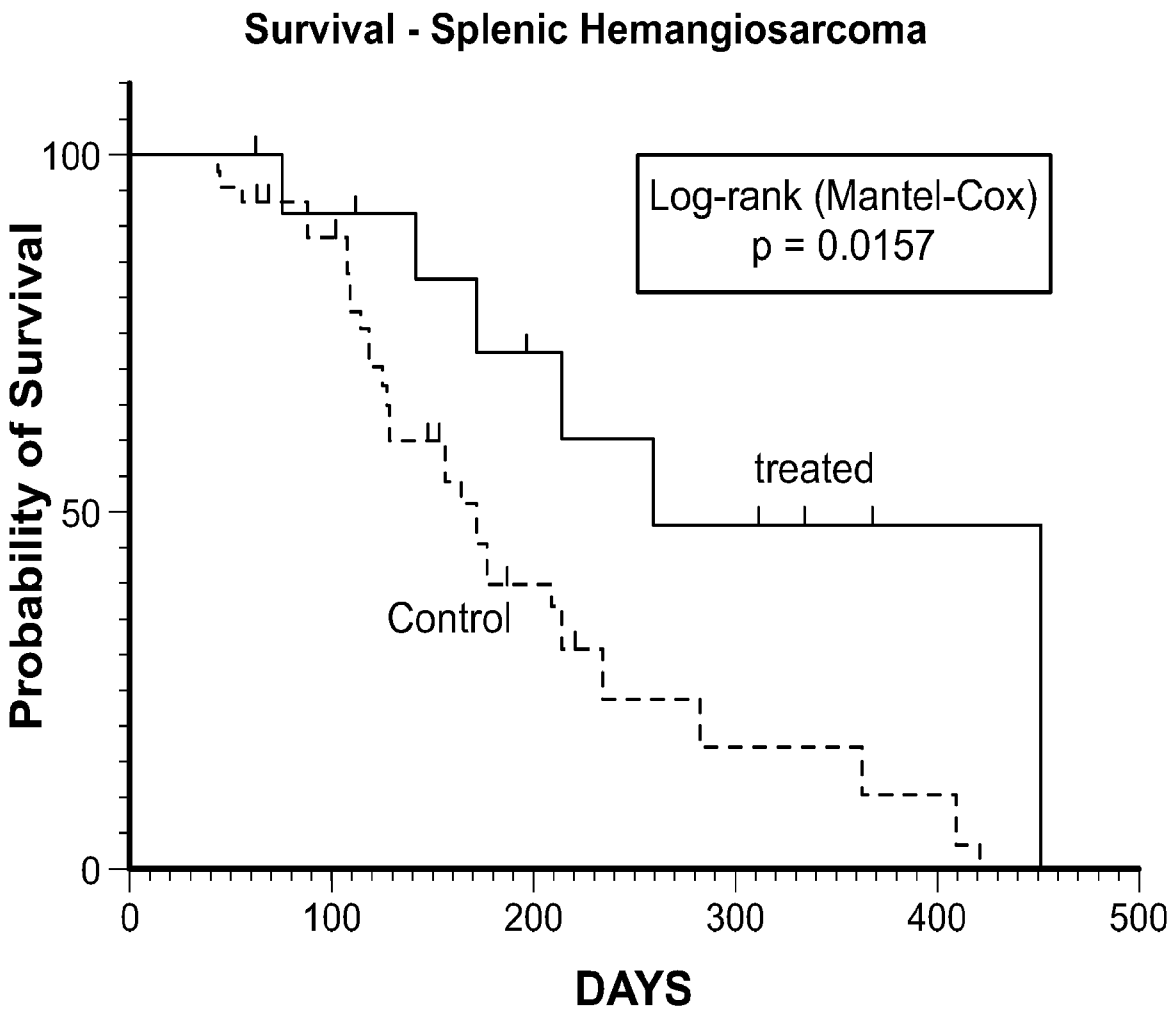

Survival of Subjects with Targetted Therapy Versus Traditional Therapy
Median Survival Time (Days)
1200
1000
800
600
400
200
0
Transitional Cell Carcinoma
Thyroid Cancer
T Cell Lymphoma
Squamous Cell Carcinoma
Soft Tissue Sarcoma
Pulmonary Adenocarcinoma
Osteosarcoma
Melanoma
Mast Cell Tumor
Mammary Carcinoma
Lymphoma
Histiocytic Sarcoma
Hepatocellular Carcinoma
Hemangiosarcoma
AGASACA
Overall
Targetted Therapy
Traditional Therapy

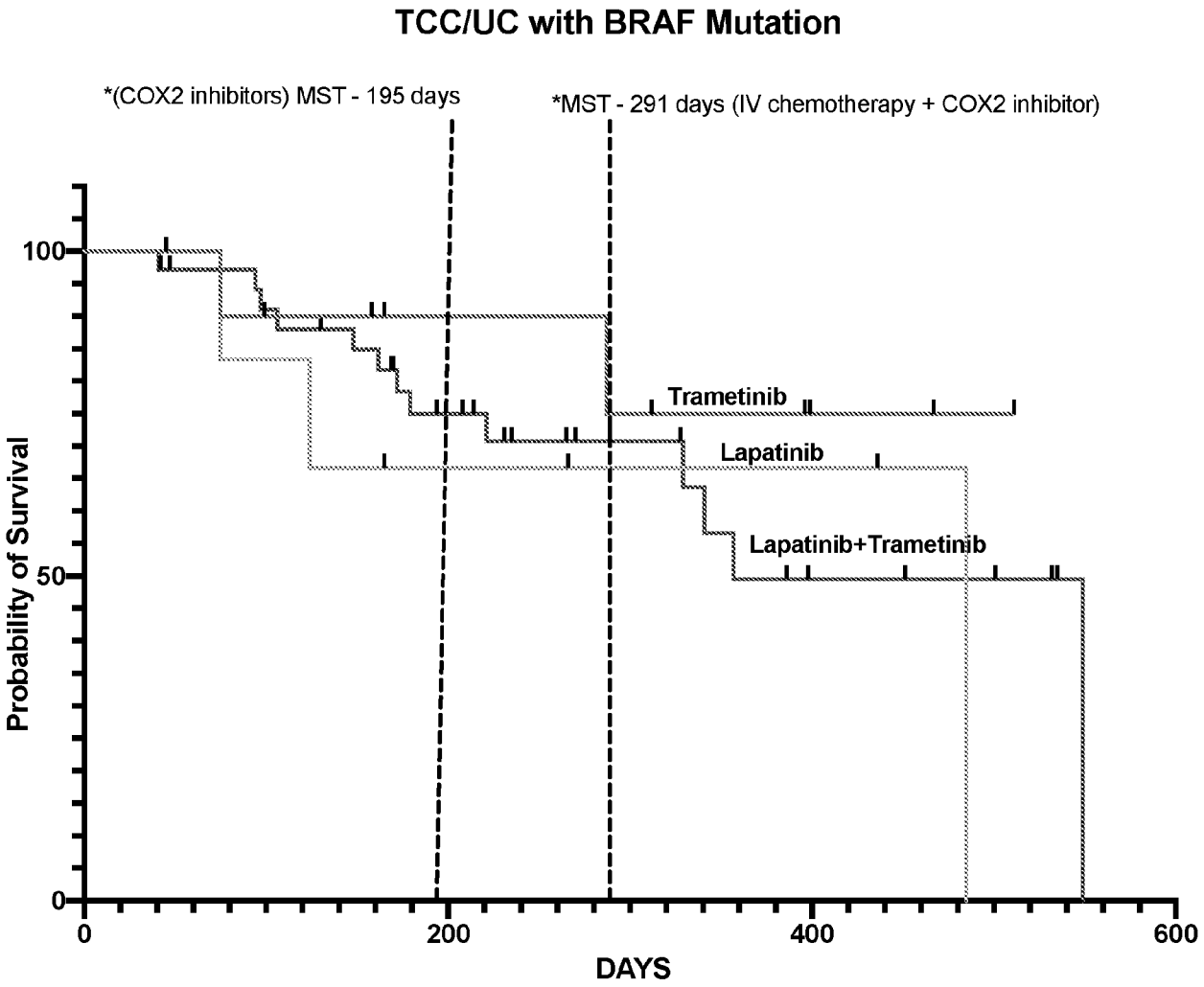
Figure 1



Control (Splenectomy + IV Chemotherapy
n = 44

Treated (Splenectomy + IV Chemotherapy + Targeted Therapy
n =13

Figure 2



* Knapp, Deborah W, and Sarah K McMillan. "Chapter 29: Tumors of the Urinary System." *Withrow & MacEwen's Small Animal Clinical Oncology*, by Withrow et al., 5th ed., Elsevier, 2013, pp. 572–582.

Figure 3

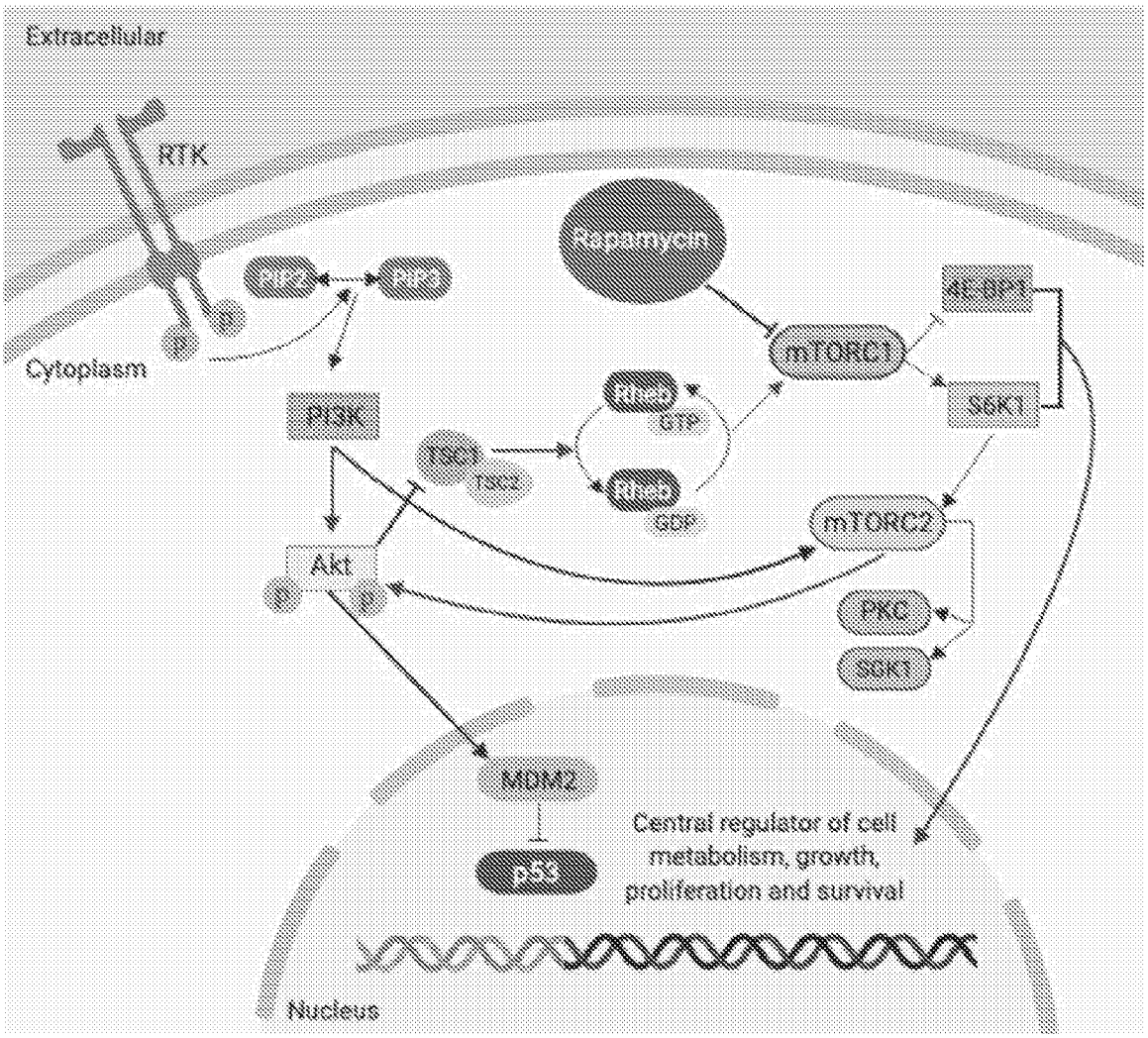

Extracellular
RTK
Rapamycin
PIP2
PIP3
4E-BP1
Cytoplasm
mTORC1
S6K1
PI3K
Rheb
GTP
TSC1
TSC2
Rheb
GDP
mTORC2
Akt
PKC
SGK1
MDM2
Central regulator of cell metabolism, growth, proliferation and survival
P53
Nucleus

Figure 4

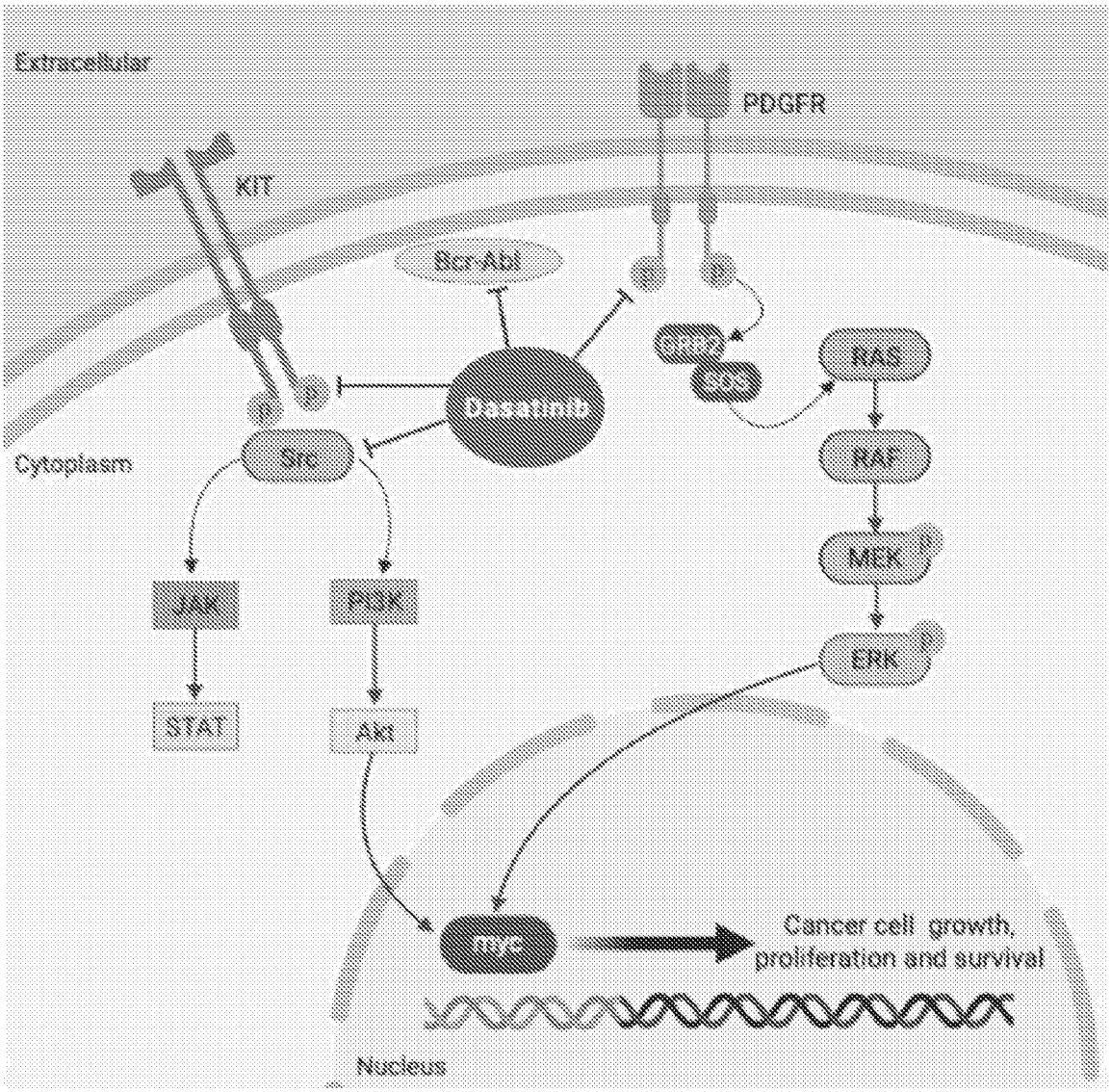

Extracellular
PDGFR
KIT
Bcr-Abl
Dasatinib
GRB2
SOS
RAS
RAF
MEK
ERK
Src
JAK
PI3K
STAT
Akt
Cytoplasm
myc
Cancer cell growth, proliferation and survival
Nucleus

Figure 5

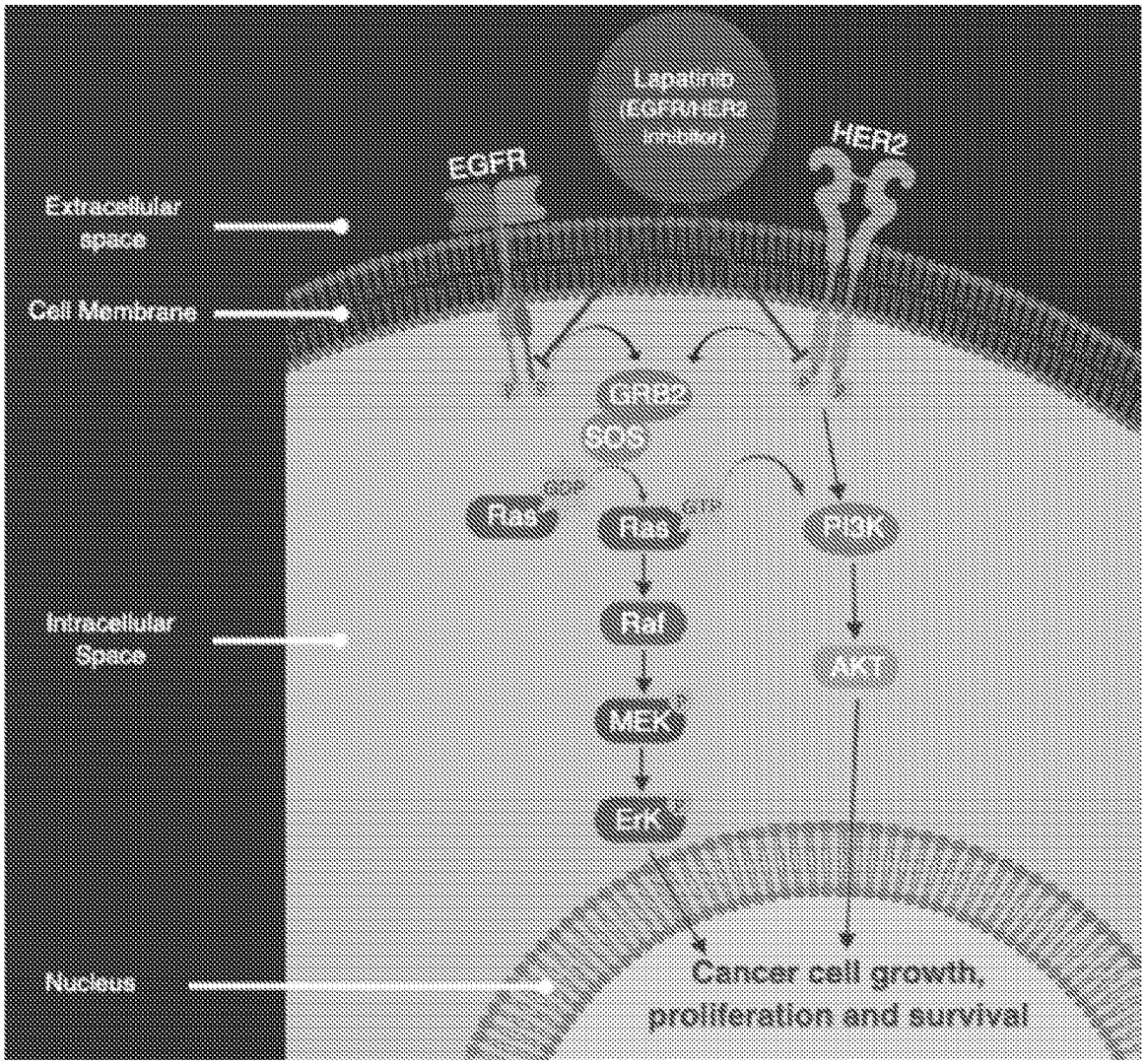

Lapatinib
(EGFR/HER2
inhibitor)
EGFR
HER2
Extracellular
space
Cell Membrane
GRB2
SOS
Ras
Ras
PI3K
Intracellular
Space
Raf
AKT
MEK
Erk
Nucleus
Cancer cell growth,
proliferation and survival

Figure 6

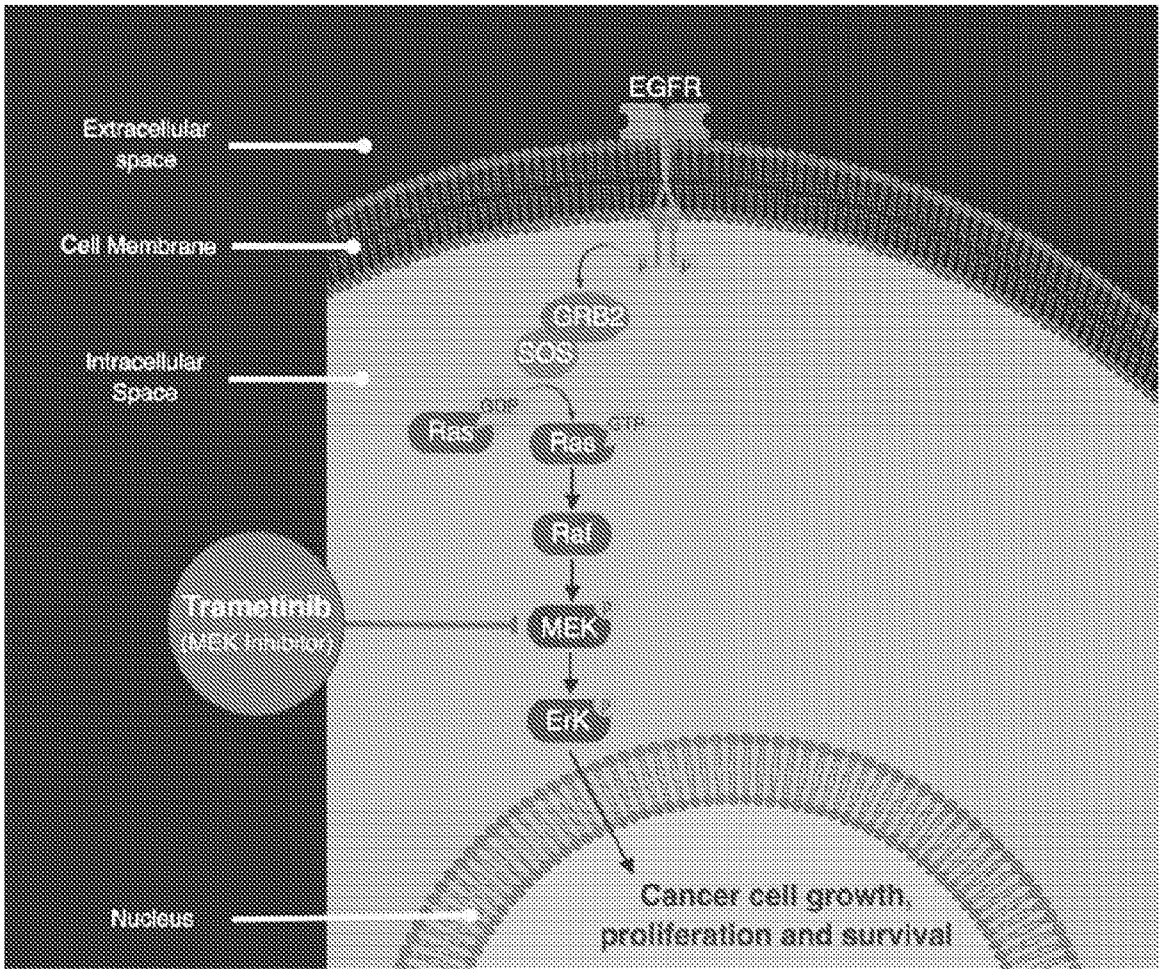

EGFR
Extracellular space
Cell Membrane
Intracellular Space
GRB2
SOS
Ras
Raf
MEK
ERK
Trametinib
(MEK Inhibitor)
Nucleus
Cancer cell growth, proliferation and survival

Figure 7

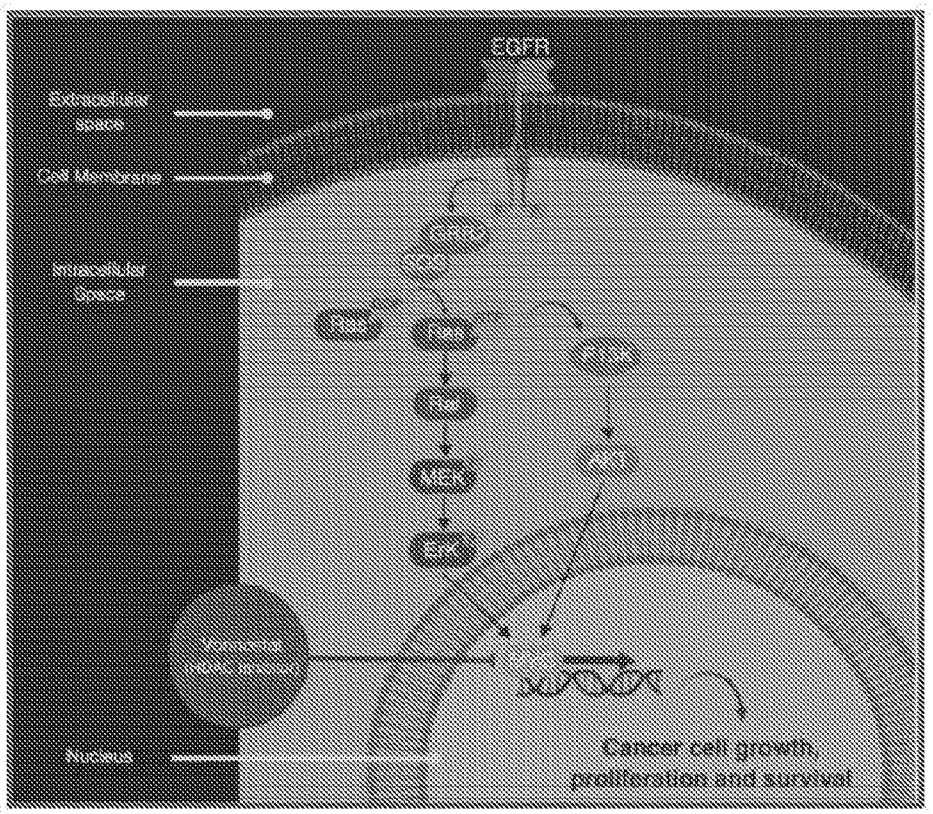

EGFR
Extracellular space
Cell Membrane
Intracellular space
Ras
Raf
Mek
Erk
Nucleus
Cancer cell growth, proliferation and survival

Figure 8

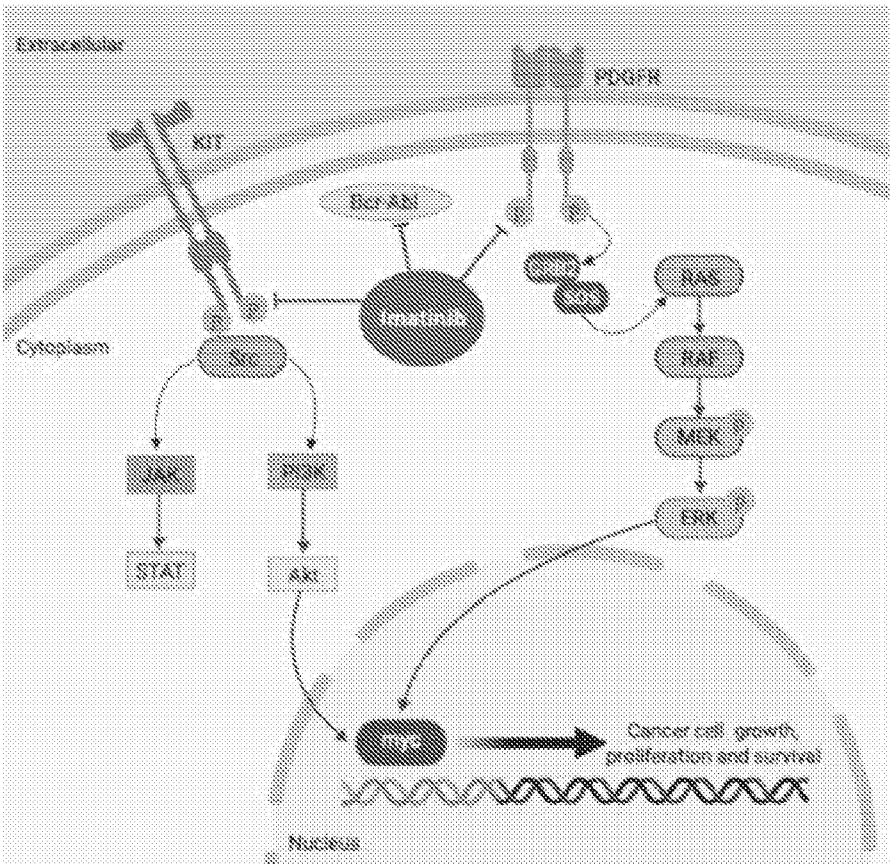

Extracellular
PDGFR
KIT
Bcl-XL
Cytoplasm
RAS
RAF
MEK
ERK
PI3K
AKT
STAT
Cancer cell growth, proliferation and survival
Nucleus

Figure 9

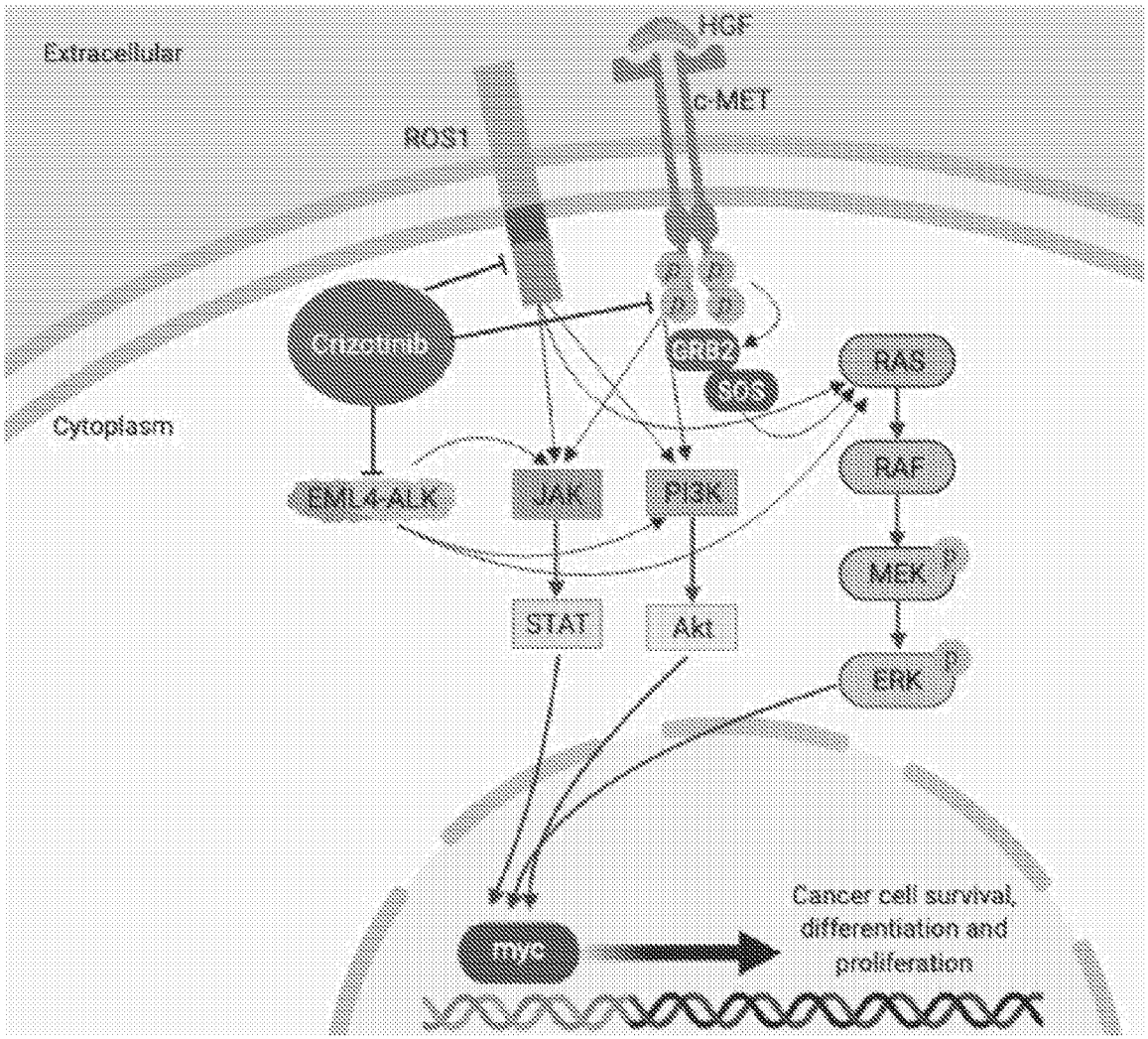

Extracellular
HGF
c-MET
ROS1
Crizotinib
GRB2
SOS
RAS
Cytoplasm
RAF
EML4-ALK
JAK
PI3K
MEK
STAT
Akt
ERK
Cancer cell survival, differentiation and proliferation

Figure 10

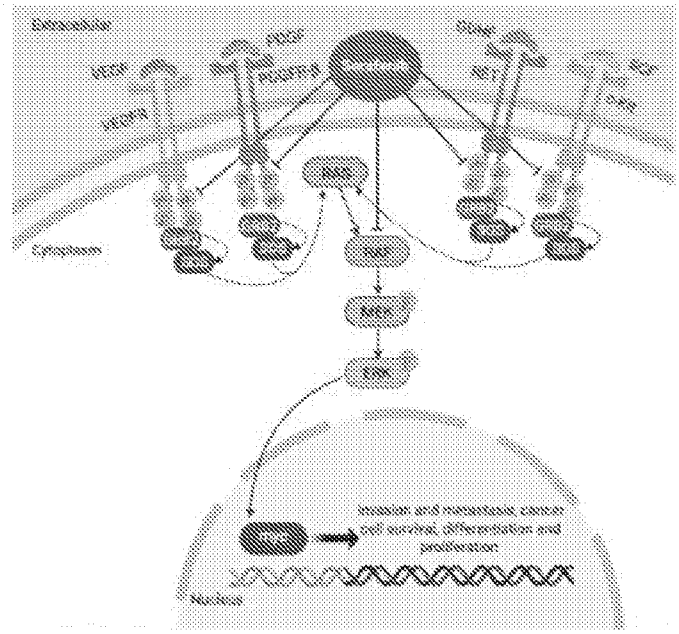

Extracellular
VEGF
PDGF
PDGFR
VEGFR
Cytoplasm
Ras
Raf
MEK
ERK
Invasion and metastasis, cancer cell survival, differentiation and proliferation
Nucleus

Figure 11

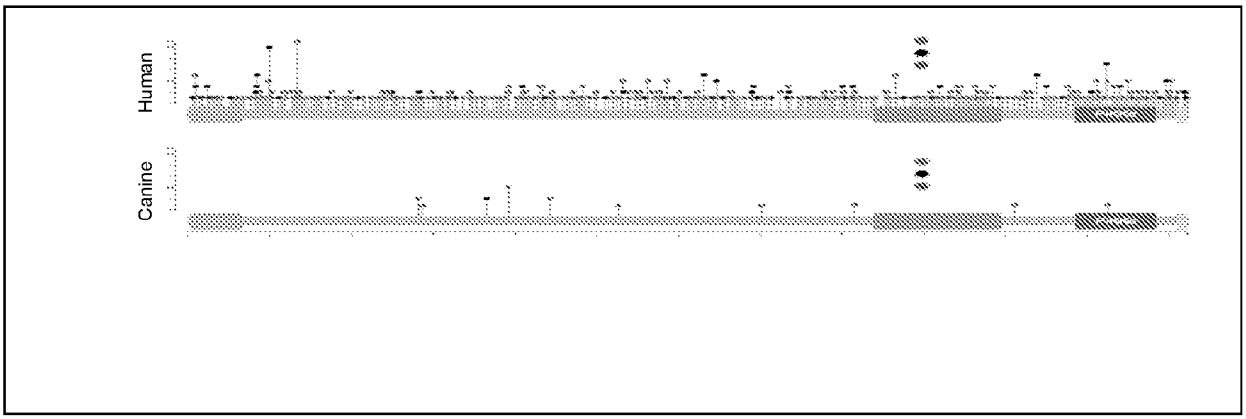


Figure 12

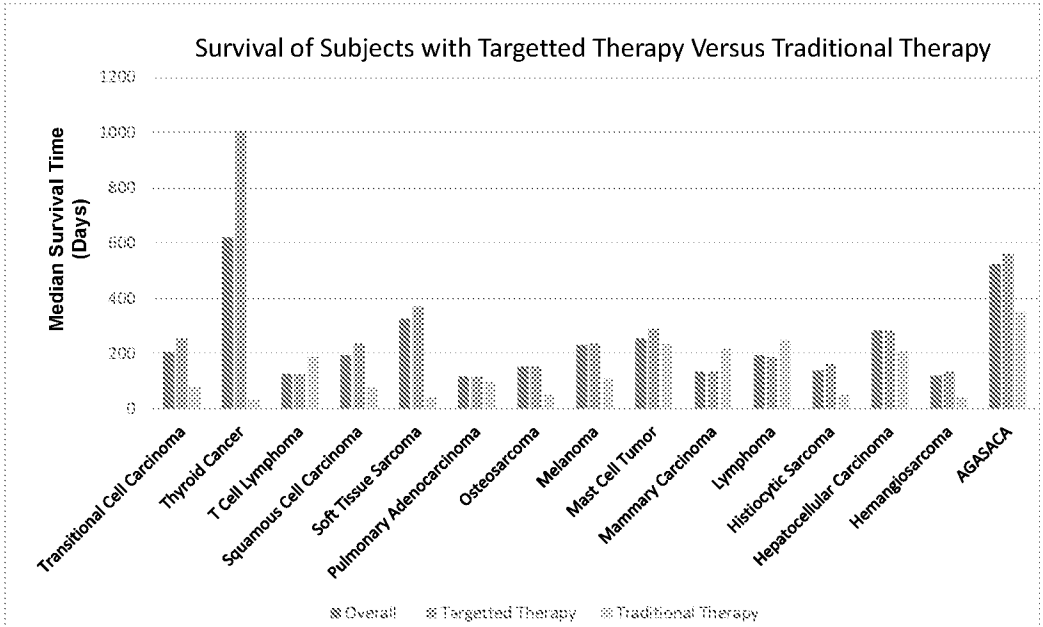

Survival of Subjects with Targetted Therapy Versus Traditional Therapy
Median Survival Time (Days)
1200
1000
800
600
400
200
0
Transitional Cell Carcinoma
Thyroid Cancer
T Cell Lymphoma
Squamous Cell Carcinoma
Soft Tissue Sarcoma
Pulmonary Adenocarcinoma
Osteosarcoma
Melanoma
Mast Cell Tumor
Mammary Carcinoma
Lymphoma
Histiocytic Sarcoma
Hepatocellular Carcinoma
Hemangiosarcoma
AGASACA
Overall
Targetted Therapy
Traditional Therapy

Figure 1