Cancer detection in 2022: Can a blood test really find 30 different types of cancer in dogs?

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Disclosures:

Dr. Andi Flory is the Chief Medical Officer and co-founder of PetDx.

Earlier this year, the CANcer Detection in Dogs (CANDiD) study was published, detailing the clinical validation of a novel "liquid biopsy" test for the detection of 30 different cancer types in dogs from a simple blood draw. Data from this landmark study, which involved over 1,000 cancer-diagnosed and presumably cancer-free dogs, will be presented. The session will review the clinical applications of this innovative cell-free DNA-based technology and provide initial laboratory experience showing how this testing is being used in veterinary practices across the country. The session will close with a series of interesting case studies demonstrating the real-world applications of liquid biopsy testing as a cancer screening tool for dogs at higher risk of cancer, and as an aid-in-diagnosis for dogs in which cancer is suspected.

Speaker Bios:

Dr. Andi Flory, DVM, DACVIM (Oncology)

Chief Medical Officer

Dr. Flory is a specialist in medical oncology with nearly two decades of experience practicing and publishing in the areas of early cancer diagnosis, treatments, trials, and novel diagnostic test evaluation. A diplomate of the American College of Veterinary Internal Medicine in oncology, Dr. Flory graduated from the Ohio State University of College of Veterinary

Medicine and completed additional training at Florida Veterinary Specialists and Cancer Treatment Center in Tampa, Florida, and Cornell University.

In 2019, she treated a small dog named Poppy for pancreatic cancer. Poppy lost her battle with the disease, but left an indelible mark on Dr. Flory, leading her to a newfound passion for cancer genomics. Soon after, Dr. Grosu tapped Dr. Flory to launch PetDx and serve as its first chief medical officer.

Prior to PetDx, most recently she co-directed the oncology internship and served as a medical oncologist at Veterinary Specialty Hospital in San Diego. Dr. Flory founded the medical oncology service at a sister hospital, Veterinary Specialty Hospital - North County. Prior to that she was a staff oncologist, resident advisor and co-chief of the oncology department at The Animal Medical Center in New York City. She has served as a principal investigator for national and international multi-site clinical investigational studies.

Dr. Flory is constantly expanding her knowledge in cutting-edge areas of veterinary medicine. She holds a certificate in genomics from The Johns Hopkins University along with certificates in cancer genomics and precision oncology, and genetic testing and sequencing technologies from Harvard Medical School. In addition, Dr. Flory is a skilled lecturer. An avid snowboarder and passionate foodie, when not keeping up with two preschoolers, Dr. Flory loves to travel, spend time with her husband, sons, their cat Mochi, and dog Cheyenne.

Learning Objectives:

1. Define "liquid biopsy" and examine how next-generation sequencing can be used to identify cancer-associated genomic alterations in the blood of dogs.
2. Examine initial laboratory experience, including: ordering trends, test results in submitted cases, and available outcome data.
3. Identify real-world opportunities for liquid biopsy incorporation into routine preventive care exams or as an aid-in-diagnosis when cancer is on the list of differential diagnoses.

Agenda:

- Background and clinical validation
- Study details and results
- Clinical applications
    - Examples of uses
    - Laboratory information
- Case Studies

Cancer detection in 2022 Can a blood test really find 30 different types of cancer in dogs

[00:00:00.24] Our speaker tonight is going to be Dr. Andi Flory. I would like to thank PetDx for sponsoring this webinar. She's going to be talking us through their cutting-edge technology for cancer detection. And we're very excited about it and very thankful to them for joining us tonight and making this available for all of you guys. So with that, I will hand it off to Dr. Andi Flory. Thank you.

[00:00:21.31] Thank you so much, Katie. Well, it's really lovely to be here this evening. Thank you so much for joining me today. As Katie said, my name is Andi Flory. I am a medical oncologist. And I'm also Chief Medical Officer for PetDx. And I get to present to you tonight, Can a Blood Test Really Find 30 Different Types of Cancer in Dogs? So stay tuned to find out the answer.

[00:00:42.43] But I suspect, if you are all here, that you probably have a pretty good idea that cancer is a big problem in the patients that we manage in clinical practice. We talk about cancer a lot with our clients. We think about it a lot. It's on our differential a lot. And that's for good reason. As you can see, here it's the most common cause of death in adult dogs.

[00:01:03.64] So this is a big problem in the patients that we manage. And in fact, 4 to 6 million dogs are diagnosed with cancer every year in the US. Now the story of our company, of PetDx, really started with just one dog. And that was little Poppy here. She was just adorable little 8-pound ball of fluff. She was mostly furry.

[00:01:23.14] I think she had these big-- you can't tell from the picture, but she had these big, floppy ears, almost like a papillon kind of vibe. But Poppy was just absolutely adorable. And like so many patients that I see in Clinical Oncology practice, she unfortunately had cancer diagnosed after she developed clinical signs. And that's what alerted her veterinarian, too, that something was going on. And by the time her cancer was actually diagnosed, it was very widespread.

[00:01:49.84] Now that feeling of being a veterinarian and having to tell this lovely family that, I'm sorry, your dog's cancer is very advanced. We can provide comfort care and palliative treatment. But there's not a lot I can do to provide cure or long-term control. It's a pretty devastating feeling. And so after the loss of Poppy-- Poppy's dad, Daniel, my client, and he's actually an MD. And he had background expertise in genomics and in liquid biopsy and developing this on the human side.

[00:02:18.67] And so this loss of Poppy was really the impetus for us to start this company to find a better way to detect cancer in dogs earlier so that other families didn't have to go through what he went through. And so here we are. Because if we really think about the way

that dogs are detected and diagnosed with cancer, and we think about that cancer management paradigm, most dogs are coming into that at the left side of this.

[00:02:45.01] They're coming in with clinical signs. And that is what alerts their veterinarian to the fact that something is going on. But unfortunately, we know that by the time cancer is causing clinical signs, most cancers are going to be pretty advanced. They're going to be in their later stages. They're not going to be that small, localized tumor in the organ of origin, which is the definition of stage 1. They're typically more advanced.

[00:03:09.43] Now when we can detect it at that earliest stage, that's when our ability to provide cure or long-term control is the highest. But when we diagnose it at later stages, that's when our ability to provide that cure or long-term control goes down. Now what's really amazing is that earlier cancer detection is possible by looking in the blood, by specifically testing for a biomarker called circulating tumor DNA.

[00:03:34.93] And this is really the definition of this term. "Liquid biopsy" is the detection of biomarkers in bodily fluids such as blood. And it gives us a way to detect cancer earlier. So that's what I'm going to talk about tonight. I'm going to talk about liquid biopsy. I'm going to talk about the science that makes this possible, which is cancer genomics; the technology that makes this possible, which is called Next-Generation Sequencing.

[00:03:57.13] And then I'm going to get into a little bit of clinical experience and when you can use this in your own patient. And of course, everyone's favorite, case examples. Now let me go back to that cancer detection paradigm. If we look at the way that cancer is typically detected, diagnosed, and managed, liquid biopsy fits into that paradigm at multiple time points.

[00:04:18.67] And these are well established on the human side. And these are called use cases. So these clinical uses, these six clinical uses are called use cases, easy for me to say. And they're roughly divided into prediagnosis and postdiagnosis. So prediagnosis means exactly what it sounds like. These are dogs that don't yet have a diagnosis of cancer.

[00:04:39.53] So liquid biopsy can be used to detect cancer in patients as a screening test that would be in an asymptomatic but high-risk population, meaning maybe higher risk because of their age or because of their breed. And that's a test that's meant to be done serially as you can see by these three little tubes that are indicated here. And then we also have aid-in-diagnosis.

[00:05:01.43] So aid-in-diagnosis is for a patient in which cancer is suspected because of their clinical presentation. But maybe it's cancer versus autoimmune, versus inflammatory. And this is a test that can help to narrow down the list of differentials, which might help to guide you as a clinician in, where do I go next in terms of the workup or the referral? So those are the prediagnosis use cases.

[00:05:24.27] Now the postdiagnosis use cases then are for dogs that have been diagnosed with cancer. These are liquid biopsy uses for helping to guide the therapy for a patient with cancer, either to help to select the best treatment, to monitor their response to cancer treatment, to determine whether cancer remains in the body following surgery that's called minimal residual disease detection, or after a patient completes therapy, recurrence monitoring.

[00:05:54.57] So after they've been through all of their cancer treatment, whether that's surgery and chemo and all of that sort of thing, this is a test that could be done to determine, is cancer coming back or spreading, which would give us an indication that patient might benefit from restarting some therapy. Now you might be wondering, well what happens on the human side? Is this available for people? And so the answer is a resounding yes.

[00:06:18.09] And this is not an exhaustive list by any means. But this is an idea of the current landscape of liquid biopsy testing that's available for people. So these are blood-based cancer detection tests. And you can see that they're divided up into these use cases. So some companies focus on monitoring a patient's response to treatment or for selecting the best treatment for an individual, determining again if cancer remains in the body following surgery.

[00:06:44.68] So that's at that MRD detection or determine if cancer is coming back or spreading, recurrence monitoring. Now the category at the bottom, I particularly think is quite exciting. This is cancer screening. So this is an asymptomatic but high-risk population. And one such company that is offering this and specifically offering a type of test called a Multi-Cancer Early Detection or MCED test is a company called GRAIL.

[00:07:10.98] So they're offering a test called Galleri, which is an MCED test. And this is now available for people. It's recommended for people over the age of 50, particularly with a family history of cancer. And it does need to be ordered by a physician. So it is by prescription. But they presented some of their data at the American Association for Cancer Research Conference last year.

[00:07:32.13] And they looked at a group of people with a preselected group of about 50 types of cancer as compared to a group of people that were presumably cancer-free, meaning no history of cancer and no current suspicion of cancer. And the detection rate in this group of people with 50 types of cancer was about 51%. And the false positive rate was very, very low, less than 1%, so a specificity of 99.5%, so really, really exciting numbers.

[00:07:58.95] Now what is important to understand about liquid biopsy, in general, is that not all cancers are created equal when it comes to being able to be detected by liquid biopsy. And some of that has to do with biology. This is a bar graph that shows detection rate by cancer type. And darker blue on the right are cases where over 75% can be detected and lighter blue on the left, less than 25%.

[00:08:24.15] Now if you think about the ability to detect a biomarker in a liquid in the body, sometimes a certain tumor in a certain location in the body might preferentially shed that biomarker into a different liquid. So if you think about the urinary tract, for example, and note that tumors that are associated with the urinary tract, like prostate, kidney bladder, they're closer to the left side of this diagram because, really, they're going to be shedding more of their biomarker probably into the urine.

[00:08:51.63] They also specifically excluded central nervous system tumors. But that would be another type of tumor that would potentially shed less biomarker into the blood but rather into maybe a different liquid like the CSF. Now I think that something to be highlighted here is that what's really exciting is that the vast majority of the tumors on this list that they can now detect are tumors that do not have a preexisting screening paradigm in people, which means that the way that most people are detected to have these cancers are when they start showing signs and symptoms by which point cancer is often very advanced. And the ability to provide cure is low.

[00:09:28.71] So this is a really exciting new ability to detect some of these very aggressive cancers earlier and potentially have a big impact on outcomes. And that's the same boat we're in in veterinary medicine as well. We don't have a screening paradigm to detect cancer early in dogs. So it means that most of our patients are detected due to clinical signs. So here again, is just this exciting new technology that's now available.

[00:09:54.78] So let's get into a little bit about the science behind how liquid biopsy works, which is really cancer genomics. So genomics is the field of science that studies an individual's entire genome. Or you can think of that as the entire set of instructions in all of their DNA. And the entire genome is present in every cell of the body, really apart from mature red blood cells. And to be able to fit in every cell, it really has to be packaged up quite condensely.

[00:10:20.45] And so just a little bit of a reminder, DNA consists of these nucleotides or bases, these paired bases that are affixed to this double helix backbone, long stretches of DNA we refer to as genes. And then DNA is wrapped around these proteins called histones, which are then used to package into structures called nucleosomes. And then this is what's used to package everything into chromosomes. And that's how everything can fit into the nucleus of the cell.

[00:10:48.72] Now, the statement at the top of the screen that cancer is a disease of the genome, what that really means is that the underlying cause of all cancer is that normal cells accumulate random alterations in the genome, so mutations in the DNA over time. And that this is really the cause of cancer. So when we have an accumulation of these alterations that confer an uncontrolled growth advantage to a population of cells, this is when cancer occurs.

[00:11:19.95] And it really starts with just a single cell developing that uncontrolled growth advantage. So in this image here, we have this little pink cancer cell. And over time, this cell is

going to grow and divide. It's going to make copies of itself. So it's going to make some clones. And along the way, it's also going to accumulate those new alterations in the genome, so those new mutations in the DNA.

[00:11:43.09] And that's going to give rise to new subpopulations of cells with their own unique set of alterations in the genome. And again, those cells will grow and divide and then give rise to new populations of cells. So by the time we actually recognize that our patient has cancer, they don't really just have a single disease. They really have multiple diseases, multiple cancers, each with their own set of unique genomic alterations.

[00:12:09.39] Now we can detect the abnormal DNA. So we can detect these alterations in the genome because there's a constant source of this DNA that we can find in the blood. So as cells die by normal mechanisms like apoptosis or necrosis, they're constantly spilling their contents into the bloodstream. And this includes all of that DNA that is present in the nucleus.

[00:12:31.98] In the bloodstream, the DNA gets broken down into fragments. And these fragments that are circulating in the blood outside of any cell are called cell-free DNA. Now cell-free DNA comes from normal cells. But it also comes from cancer cells. And that subset that comes from cancer cells we call circulating tumor DNA or ctDNA.

[00:12:56.04] So these little fragments can be sequenced and analyzed with a technology called Next-Generation Sequencing. And I like to compare this to taking those little bits of paper that come out of the paper shredder, figuring out, where does this little bit, this little fragment fit in the genome? And then we can look at the genome to figure out, do we see changes there that are consistent with the presence of cancer?

[00:13:22.71] We can see changes that are way down just at the single nucleotide level. We can see changes that are way out here at the gene level. Or we can even see changes that exist way out here at the chromosome level. Because if those changes are found, those are not changes that we see in normal individuals. And they're not changes that we see with conditions like inflammation, infection, autoimmune disease.

[00:13:47.68] So when they're found, that's a unique signature. And it's a unique indicator of the presence of malignant tumor cells in the body. It's also important to note that these little fragments are very short lived in the body. They only last minutes to hours. So the blood sample has to be collected into special blood collection tubes to stabilize the blood cells and stabilize those delicate little fragments of DNA.

[00:14:12.42] So this is kind of a little cartoon of how the process works. So normal cells and cancer cells are shedding DNA into the bloodstream. The specialized blood collection tubes are used to collect the sample at the clinic. And those tubes help to stabilize the sample for seven days at room temperature without any need for refrigeration, freezing, spinning, anything like that.

[00:14:33.65] The sample is then overnighted to the lab, where the blood is then separated out into components. The DNA is extracted and amplified, which means make lots of copies and then sequenced on these big fancy machines called NovaSeq 6000 that look a little bit like a really big washing machine with a screen on it. But they're very, very fancy machines.

[00:14:55.82] And then it's the job of the data scientists called bioinformaticians to go through the billions of data points that are generated for every single patient to look for those spelling mistakes in the DNA that should not be there, which is an indication of tumor cells present in the body. And so that's a really, really high technology.

[00:15:16.97] But we can boil this down to a few easy concepts when we talk about how liquid biopsy works with dog owners, for example, which is that cancer is caused by certain abnormalities in the DNA. There's a non-invasive test called liquid biopsy that can detect these abnormalities in the blood and that the detection of these abnormalities in the blood indicates the likely presence of cancer.

[00:15:42.17] So how do we really know this works in dogs? Well, we performed a very robust clinical validation study that I'd love to go over with you now. And if we go back to those use cases, the clinical validation was really looking at detection of cancer. And really, that's most applicable to these prediagnosis use cases, so screening a dog for the presence of cancer and use as an aid-in-diagnosis in patients for which cancer is suspected.

[00:16:11.20] So the cancer detection in dogs or CANDiD study is the name of the clinical validation study. This has been peer-reviewed and was published in a journal called PLOS One in April of this year. The study was performed at a variety of different clinical sites, as you can see on the lower left here. And we ended up enrolling over 1,700 dogs into this study. And I think that really just highlights the absolute enthusiasm that veterinarians have.

[00:16:40.44] I think that there's just this general feeling of, you mean to tell me, all of these years, clients have been asking me, isn't there a blood test for cancer? And now I might be able to say yes? So I think that there was just a lot of enthusiasm around the idea for a study like this. But also, dog owners, I think, are just really so willing to give back and to pay it forward and help future dogs with cancer.

[00:17:02.56] So there's a ton of enthusiasm for enrollment into the study, which we're incredibly grateful for. So we ended up enrolling over 1,700 dogs into the study. And these dogs were enrolled into one of three protocols. Protocol 101 on the bottom here were dogs that were presumably cancer-free. And what this meant was that these were dogs that had no history of cancer.

[00:17:23.07] There was no current suspicion of cancer based on a thorough history and physical exam by the enrolling veterinarian at the time of enrollment. Importantly, these dogs were allowed to have common skin and subcutaneous tumors, like lipoma, skin tag,

sebaceous adenomas, things like that. And they were allowed to have any number of acute or chronic medical conditions. They just couldn't have a suspicion of cancer.

[00:17:46.42] So this was a very real-world population of dogs. These dogs had everything from atopy to diabetes to Cushing's to myositis to all kinds of skin conditions and dental disease, very, very real world population of dogs. And the dogs that were in the 201 and 301 cohorts, these were dogs that had confirmed cancer. But again, they were also allowed to have these other conditions. So again, very real-world populations of dogs in all of these cohorts.

[00:18:21.25] Now when we were ready to perform the validation itself, we had 1,100 dogs that were eligible for the validation testing. 1,100 dogs is just so much larger than most studies that I have seen that. So it was just so exciting to see this really absolutely huge number to perform this validation. These dogs represented 85 different breeds over 40 types of cancer.

[00:18:47.66] And these were enrolled at 41 clinical sites around the world. And this was a huge brain trust that made this project possible. There were 39 veterinarians, 21 of which were specialists, 14 PhDs, and 3 MDs that came together. And it's really this amazing collaboration between human and veterinary researchers that really made this possible, so really exciting study.

[00:19:10.82] Now, one thing that is important to note is that these dogs were randomly assigned to a training set and a testing set. And so what this is for is a training set in diagnostic test development is really where you teach the test what to call cancer and what not to, so really to develop the algorithm. And then once the algorithm is locked down, use that in a blinded fashion on the testing set. And then that is where test performance is determined.

[00:19:37.69] It's important to do this to prevent something called overfitting. And that essentially is, say, we had just used one big testing set of 1,100 dogs. The risk of using that to also determine what is cancer and what is not and also analyze test performance is that when you use that in a real-world population, you really risk the test almost seeming too perfect of saying what is cancer and what is not.

[00:20:02.06] And so when you use it in a real-world situation, it doesn't really perform the same way. So that's why this is done is really, this is best practice in diagnostic test development. So we still had about 900 dogs that were in the testing set, so a very, very large number. And so when we go and start to look at how well the liquid biopsy test performed, we started by looking at the specific cohorts of diseases.

[00:20:26.93] And we really wanted to start with, what are the three most aggressive cancers that we see in dogs? So those are in this little pink triangle here. So dogs that had one of these three diagnoses-- lymphoma, hemangiosarcoma, and osteosarcoma, the liquid

biopsy test had a detection rate of 85%. So 85% detection rate by OncoK9 with these three very aggressive cancer types when we add in another five cancers to round out the eight most common cancers that veterinarians see, diagnose, and manage in clinical practice.

[00:21:01.25] So adding to the top three-- mast cell tumor, soft tissue sarcoma, mammary gland carcinoma, anal sac carcinoma, and melanoma, we have a detection rate of 62%, so 62% in the most common cancers that veterinarians see. And then when we look at the all-comers cohort representing over 40 types of cancer, the detection rate across all groups was 55% with a very high specificity across the entire study of 98.5%, meaning a false positive rate of only 1.5%, which is really, really exciting.

[00:21:36.79] Now here is a list of the 30 types of cancer that the test was able to detect. So remember that question at the top of the hour? Can a blood test really detect 30 types of cancer? The answer is, it can. So these are the 30 types of cancer that the test could detect. And what do I mean by type?

[00:21:54.59] So if you look at this list, you'll see that this list is actually put together with most of these cancers being listed by anatomic location. The reason for that is that generally, when veterinarians are working up a patient, they don't know the specific histologic type of cancer that their patient has. But they have a good idea of where in the body it may be coming from. So that's the primary reason for doing that.

[00:22:17.59] Now some of these are listed by histologic type. This tend to be cancer types that might be multisystemic, might happen in more than one part of the body, or may be the only type of histology that really occurs with any frequency in that particular anatomic location. So that's why that list is put together in a unique way.

[00:22:40.80] Now in certain circumstances, you may suspect a particular type of cancer based on your patient's presentation. And so sometimes, cancer-specific test performance might be helpful. So shown here are the individual detection rates for those eight most common cancer types. So what we can see here is that just like in the GRAIL data, not all cancer types perform the same.

[00:23:03.73] We can see that some cancers have higher detection rates like those kind of three most aggressive cancers are towards the left of the screen here. And then you have towards the right side of the screen, some that have lower detection rates-- soft tissue sarcoma, mast cell tumor, anal sac adenocarcinoma. These are cancers that tend to be found on physical exam.

[00:23:24.12] A lot of times they are found early in the disease process, meaning when they're small and localized and easily accessible as a small localized skin tumor for direct sampling. And so these are cancer types where you're probably, as a veterinarian, going to get more clinical information from a tissue biopsy than a liquid biopsy, so just something to keep in mind when you're thinking about patient selection for this type of technology.

[00:23:53.29] Now finally, just as not all cancers are created equal when it comes to type-- ability to be detected by liquid biopsy, in addition to that, not all cancers are created equal when it comes to tumor size and extent and ability to be detected by liquid biopsy. So what we're looking at here are, these dogs were divided into stage classes based on extent of disease in the body and then also, further separated by size.

[00:24:19.66] So dogs that had localized and regional disease which are the left two most columns here were patients that had cancer that was isolated to the organ of origin and/or a nearby lymph node. And then in the right two columns we had dogs that had cancer that was spread beyond that local lymph node, so disseminated metastatic. And then in the middle here, this category is for cancers that don't neatly fall into one or the other, just undocumented or not really able to determine a size for that particular cancer.

[00:24:50.36] So what we can see here is that dogs that had disseminated metastatic disease, OncoK9 was able to detect 83% to 88% of these. And for localized and regional, we have for larger tumors that were localized and regional, detection rate was over 50%, and for smaller tumors was about 20%. And in the middle, we have this undocumented.

[00:25:13.51] Now 20% might not sound like a lot. But if we consider what is the current paradigm, a recent study that we performed indicated that dogs with cancer were detected on a wellness exam only 3% of the time and incidentally while being monitored for another disease, only 8% of the time. So this number, even though it seems low, for the smallest extent of disease, the detection rate of 20% for even the smallest tumors is a huge improvement over our status quo and our ability to detect cancer early in our patients now.

[00:25:47.62] So really exciting to think about what this could mean for really moving the needle for patient outcomes by detecting them earlier. Now I want to jump into the test process itself a little bit. So you can just have an idea of what is involved. And again, remember that the validation was performed to validate cancer detection. And that's most applicable to these prediagnosis use cases.

[00:26:10.48] So most of the time, when you're performing the test, you're probably going to be performing it for one of these two reasons-- either as a cancer screening test in a dog, where you do not currently suspect cancer but maybe is at higher risk of cancer, or as an aid-in-diagnosis for a dog in which you do suspect cancers on the differential list.

[00:26:31.46] Remember that we also need to use those special tubes for this test. So you do need to obtain a kit. You can get a kit from PetDx or from our diagnostic distribution partners like IDEXX or Antech. And here are the contents of the kit. So this contains these specialized blood collection tubes. These are cell-free DNA optimized blood collection tubes that contain a preservative that stabilize the blood cells and stabilize the DNA for seven days at room temperature.

[00:26:59.88] The only special handling that you need to do is just adequately mix that sample to make sure that the blood does not clot. This should never be refrigerated or frozen as that will destroy the sample. So really, you don't need to fuss around with finding an ice pack and a foam cooler and all of that stuff. You just really can pop it back in the box and ship it.

[00:27:19.49] Now in addition to that, we also provide a way to pull the sample directly from the patient's vein right into the tube, just like if you or I were to go to Quest or LabCorp today. This is how they would pull our blood. It's a very convenient way to pull multiple tubes at once. And in fact, the majority of techs that we educate on this system end up really loving it and want to use it for all of their patients. So just beware it could make your tech's life easier by learning to use this system.

[00:27:47.39] Now in terms of volume, if you note here on the tube, you'll see these little black lines that are on this label. These are the minimum and the maximum fill lines. Both tubes have to be filled to above that minimum fill line; otherwise, the test cannot be run. And that minimum fill line is 7 mLs. So 7 mLs times 2 tubes, it is a minimum of 14 mLs and a maximum of 17 mLs. To put it into perspective, that's about 1 tablespoon.

[00:28:15.60] This is a very, very safe volume of blood to draw on the vast majority of canine patients that you see down to around a body size of just under 2 kilograms. Now what happens then after you pull the sample? So you pull the sample at your clinic. It either gets handed off to the courier or it gets put back into the kit and overnighted through a prepaid FedEx label. It is overnighted to our lab, where the sample is processed.

[00:28:43.63] The DNA is extracted in our lab in San Diego. All of the steps, including library preparation and sequencing and data analysis are performed by our team. And then there's a lab team review. And then a report is issued back to the veterinarian. Now what does that report look like? Well, the test result is a qualitative answer. It is a yes/no.

[00:29:06.42] It is where those alterations in the genome-- so the genomic alterations detected in this patient's blood sample or not. And we call that a cancer signal. So in the case of the top result here in green, this is cancer signal not detected, which reduces the likelihood that cancer is present in this patient. But it does not rule out the presence of cancer because false negatives can occur, of course.

[00:29:31.17] And so if cancer is still clinically suspected in your patient, then a full diagnostic evaluation should be performed. So that's important to keep in mind. In the case of a cancer signal detected result, this significantly increases the likelihood that cancer is present. But this is not a diagnostic test. It doesn't confirm the presence of cancer.

[00:29:49.99] And so important decisions like treatment or euthanasia should never be made on the basis of this test alone. This is a screening test. So it means that a positive test

should always be followed by a confirmatory cancer evaluation to establish that definitive diagnosis.

[00:30:06.72] Now, what does it really mean in terms of what you should do as next steps when you get that positive result? So included on the report are, what is recommended as a next step. Every patient that gets a positive test result gets support from our clinical support specialists. So they reach out to every veterinarian that submits a test that they get a positive result and helps them understand what should you do next in the case of this patient in terms of the workup.

[00:30:34.49] If you perform this test as an aid-in-diagnosis, your workup is very much going to be guided by what's going on with that patient and what you suspect is going on. And so your workup will be guided by that. But what if you perform this test as a screening test? If you perform this test as a screening test, then you're going to want to go on this what I call the cancer hunt. You're going to want to try to find where is this cancer signal coming from.

[00:30:59.66] Some suggestions of what would be recommended would be a very thorough history, so really questioning that family, what's going on with this pet; a very thorough physical exam, remembering to look in the mouth, do a rectal exam, palpate the ventral neck, palpate the lymph nodes; full lab work like CBC/Chem/UA, imaging of the chest and the abdomen and any areas of bone or joint pain.

[00:31:22.40] And then sample anything you find. So aspirate lumps, bumps, enlarged lymph nodes, lesions on ultrasound; look for where can this signal be coming from. And when you get this test result back, what does this really mean? So, so far, we've really been talking about the test itself. We talked about the clinical validation of the test. When we talk about the test, the important test metrics are really sensitivity and specificity.

[00:31:48.34] But when you've done a test, and now you have this test result in front of you for this nine-year-old golden retriever that you've just tested, what does that mean for that dog? And how do you interpret it? So now what arguably becomes more important is the positive predictive value, so not so much the sensitivity and the specificity alone but also determining what the positive predictive value is.

[00:32:12.04] And there's a standard formula that's listed at the top of the screen here. And if you know, it takes into account the sensitivity. It takes into account the specificity. But it also takes into account the prevalence. And so the prevalence is a little bit of a tricky to pin down. In people, that's well known because cancer is a reportable disease. So prevalence is very clear. And that's not the case in dogs.

[00:32:35.47] So we went through an exercise to estimate what is the prevalence. And so now we have to think about, well, why am I running this test? Am I running this test as a screening test? Or am I running this test as an aid-in-diagnosis? Because the prevalence is

different in these two populations. The prevalence of cancer is different if you're performing this test in a screening population, where this is an asymptomatic but maybe older dog or a breed that's known to be at higher risk of cancer.

[00:33:03.50] And so using population data in the US and the number of cancer diagnoses each year in the US, about 6% to 7% of dogs are diagnosed with cancer every year. Looking at a higher risk population of older or certain breeds, we know that the prevalence is going to be a little bit higher than that. So we estimated that to be around 8% to 10%. On the aid-in-diagnosis side, by the time a veterinarian is suspecting cancer, by the time cancer is on the differential list, the prevalence in that group is higher. It's about 30% to 50%.

[00:33:36.11] So now when we go through this exercise, we can actually plug these numbers into the population to determine what is the PPV for these two different populations of dogs. So if we look down the left side here, when you're running this test as a screening test and you get a positive test result back, the PPV is 76% to 80%. And what PPD really means is, what is the probability or what is the chance that that dog has cancer if you get a positive test result?

[00:34:05.42] So for that nine-year-old golden that you've tested and you've done this as a screening test and you get a positive test result, there's a 76% to 80% chance that that dog does have cancer, really highlighting the importance of the next steps, which is the workup to find where is that cancer. So we can get treatment started sooner.

[00:34:24.46] If we run down that sort of same process on the right side here for aid-in-diagnosis, so for a patient that you do suspect cancer and that's why you run the test, if you get a positive test result back, you can see the PPV is even higher. It's 94% to 97%, meaning that the majority of patients that receive a positive OncoK9 result will prove to actually be diagnosed with cancer, whether you're doing this as a screening test or as an aid-in-diagnosis test.

[00:34:51.82] But in thinking about interpreting the results for your specific patient, you just need to think about, why did I do this test in the first place? And that will help you understand how likely is it that this patient does have cancer. Now we can run through that a little bit faster on the negative predictive value side. I think that veterinarians rely on negative results a lot to help them understand what's going on and make decisions. So I think this is important to think about too.

[00:35:17.11] So if we run down that on the screening side, you can see that the negative predictive value is 95% to 96%. And that's really a good peace of mind when you're running this as a screening test for those high-risk dogs, 95 to 96% chance that that dog does not have cancer. On the aid-in-diagnosis side, the NPV is 68% to 84%, meaning, are there going to be some dogs that get false negatives? Yes.

[00:35:42.12] I mean, can false positives happen? Yes, it's going to be pretty uncommon. But these are important numbers to help you as a veterinarian feel comfortable about how to interpret the test results for your specific patient. Now one final thing that I'll say about the report itself is that the vast majority of patients are going to get this yes/no answer. They're going to get this cancer signal detected or cancer signal not detected, so a qualitative answer.

[00:36:07.49] In addition to that, in some cancer types, we can determine what's called a Cancer Signal Origin. And if that's present, it will be here in the common section. And so you can see on this patient's report that it says, Cancer Signal Origin prediction hematological malignancy, likely lymphoma. So most dogs are going to get this yes/no, this badge here that says cancer signal detected or not detected.

[00:36:31.70] But then some dogs will also get this Cancer Signal Origin prediction. Right now that is available for hematological malignancies like the lymphoma and leukemia, which is present in about 40% of dogs with lymphoma. But I am optimistic that won't be able to add additional Cancer Signal Origin prediction soon. So stay tuned for that.

[00:36:54.61] Now let's look at how veterinarians are using the test and what kind of results they are getting. So what we did is we took a series of-- we said we're just going to take the next 500 cases that come in. And we're going to do some additional analysis on them. So we had 500 consecutive cases that had OncoK9.

[00:37:14.74] And we found that 65% of those were submitted as a screening use case, meaning asymptomatic dogs where the veterinarian did not suspect cancer. But they were running the test to screen them because they were at higher risk either because of their age and/or their breed. 30% were submitted as an aid-in-diagnosis when cancer was suspected. And the remaining 5% were submitted for other indications.

[00:37:41.23] And that was really those postdiagnosis use cases, so recurrence monitoring or a minimal residual disease detection, for example. Looking at the results, we found that there is a positivity rate of about 13%. And of those 64 positive results, 6 of those received that Cancer Signal Origin or CSO prediction of hematological malignancy. So you can see how often that sort of prediction occurred in that cohort, which meant that 84% of results were negative.

[00:38:14.86] And less than 3% of results were not clearly negative and not clearly positive. This is called indeterminate, where there are some changes. There's what looks like it could be a cancer signal. But it's not strong enough to call a positive. And it's not negative enough to call a negative. And so when that happens, an immediate courtesy redraw is recommended.

[00:38:37.81] And so you can see that of the patients that did ultimately have a redraw, we were able to get to a definitive answer on the second test. Three of those came back as positive. And six of those came back as negative, just highlighting that if you do get this

indeterminate, don't get discouraged. This is a very small percentage of the time that this occurs. But it is important to go ahead and submit a second test. But you can see the vast majority of these results were negative.

[00:39:06.32] Now, if we break these out by use case, by how these were submitted, if we look at the aid-in-diagnosis population in the left, in purple, we can see that the positivity rate here was 26%. And 3 of the 39 cases received that CSO prediction of hematological malignancy. And on the right side, as a screening, there was a positivity rate of 6.5%. And 2 of the 21 received that CSO prediction of hematological malignancy.

[00:39:36.13] Now I have to say that these numbers were pretty exciting to our team because if we take these numbers and we really think about that the test can detect overall a 55% of all cancers or 62% of the most common cancers and we do some calculations, we get to a pretty similar estimated prevalence to those estimated prevalence numbers we used in the PPV calculation, so around 50% on the aid-in-diagnosis side and around a 10% to 12% on the screening side.

[00:40:14.62] So I'm really just highlighting that the actual real-world prevalence seems to be bearing out in those estimations. Now what happens then when these patients do go forward and get that confirmatory cancer evaluation? So those patients that have that positive test result from these consecutive cases that we looked at and had a complete confirmatory cancer evaluation, what happened with those?

[00:40:39.27] Well, what's really interesting is that of the patients that had a full workup, we found that-- we detected cancer. Or the veterinarians ended up detecting or diagnosing cancer in the majority of these. So in aid of these definitive tissue diagnosis of cancer, you can see the cancer types in the upper right here. And in 20 of these, these were presumptively diagnosed. And most of these were imaging diagnosis.

[00:41:06.63] Here, there are 20 of these. So in total, it meant 28 of 83 patients were definitively or presumptively diagnosed with cancer, meaning this is a real-world Positive Predictive Value or PPV of about 85%, so meaning that veterinarians are really finding cancer most of the time after receiving a positive OncoK9 test report. Now finally, I want to close with, when can you use this in your practice and then some case examples before we jump into some questions.

[00:41:40.59] So one thing that I want to say is that when we think about using this test as a screening test, the question is, well, when should I start using this? When should I be recommending this to my canine patients? And we wanted to have a very evidence-based answer to that. So we performed a study.

[00:41:56.93] This is a retrospective study that's been published on bioRxiv and is currently undergoing peer review with the leading peer review journal right now. This is a study in over 3,000 dogs representing over 120 breeds and over 40 cancer types to determine in this

large group of dogs when are they typically diagnosed with cancer because that can help us understand when should we start cancer screening.

[00:42:22.01] What we found is that in this group of 3,400 dogs, the median age at diagnosis was around 9 years, was 8.8 years. And probably, unsurprisingly to many watching this is that certain breeds did have an earlier median age of diagnosis. So there were certain breeds that tended to get cancer earlier. Now because we know that cancer does not happen overnight, we don't want to just start cancer screening at the time where the peak incidence occurs.

[00:42:50.09] We really want to start screening prior to that so that we have the best chance at catching it early. And so a prudent recommendation is to start that cancer screening about two years prior to the median age at diagnosis. And so if we consider the entire group where the median age at diagnosis is around nine years, that means the recommended age to initiate cancer screening for all dogs is at age seven.

[00:43:14.12] But because there are some dog breeds that get cancer earlier, then as early as age four for certain breeds. So we think about when to use the test, it's really recommended as an annual screening test. An annual because that's what fits into the paradigm of care for most dogs when most dogs are seeing their veterinarian for wellness visits. So as an annual screening test, it's recommended for dogs at higher risk of cancer.

[00:43:41.18] The dogs that are at higher risk of cancer are dogs that are older and the dogs that belong to certain breeds that are known to be high risk. The dog breeds that are known to be high risk are listed here. And I bet if you closed your eyes, you could probably guess about 90% of these right off the bat because these are the dog breeds that get a lot of cancer.

[00:44:01.59] These are the usual suspects. You've got your goldens and your labs and your boxers and your shepherds, rottweilers; some smaller dogs, beagles and frenchies. You have the dog breeds that I see a lot as an oncologist-- Bernese mountain dogs and flat-coated retrievers. And then you have dogs like Rhodesian ridgebacks and huskies. And depending on what part of the country you're in, you might see a lot of those.

[00:44:26.60] And then, of course, on the right side of the screen, we have giant breed dogs. These are dog breeds that certainly get more bone cancer. And so these are all dog breeds that are at the highest risk of cancer. And these are really the dog breeds that you want to think about when you think about, who should I be screening for cancer?

[00:44:45.53] Now the second question is, when should I start screening for cancer? So remember that I said that it makes sense for all dogs if you remember one age, remember the age of seven because that's really the age that all dogs should start cancer screening. However, because there are some breeds that get cancer at an earlier age, there are some breeds that should start cancer screening earlier.

[00:45:07.20] So if you look on the right side, for example, you see these giant breed dogs. A lot of these should start screening closer to a younger age as young as age four, boxers as young as age four. You can see that some of these are listed as five and six. And then there are also breeds, this is a separate list of dogs that may not be at the highest lifetime risk. But if they get cancer, they get cancer younger.

[00:45:30.59] And so these are breeds that if you have a family that really is looking into cancer screening, that starting at an earlier age for these breeds would be a good idea. Some of these were very surprising to me, like chihuahuas at six years and bostons at six years and vizslas at five. So these are breeds that if they get cancer, they tend to get cancer younger.

[00:45:53.33] Now fortunately, you don't need to memorize all of this. We actually have a tool that can help you. So this is called the Cancer SAFE tool. And that's actually a QR code. So if you want to take a picture of that with your phone, it should open up a link. And I'll take you right to the tool. Or you can visit cancersafe.petdx.com. So SAFE stands for Screening Age For Early detection.

[00:46:17.55] This is a tool that allows you or your owners to go on and input their dogs' or your own pet or your patient's breed and weight and determine, when should I start screening for this particular dog? What is the best age for this particular dog to start screening? So Cancer SAFE tool, check it out and learn when your pet or when your patient should start cancer screening.

[00:46:44.21] Now let's look at a case example of OncoK9 being used as a cancer screening tool that can maybe solidify this. So this is little Molly. And Molly has an owner that is worried about cancer. She's coming in because her other dog which happens to be Molly's litter mate just died of cancer. And she really wants to know, what can I do for Molly? This is a very common question that I get as an oncologist. What can I do for my other dog?

[00:47:09.20] So at the time of her testing, there was no suspicion of cancer by her veterinarian. There were no findings on her physical exam. But unfortunately, her OncoK9 test came back as cancer signal detected. So next step is confirmatory cancer evaluation. So she had a confirmatory cancer evaluation. Her physical exam and her labs were unremarkable as were her thoracic radiographs. But on her ultrasound, we've got some problems.

[00:47:35.57] We've got multiple flavors of nodules in her liver. We've got a couple of nodules in her spleen, which may be benign. And she's got a few big lymph nodes next to her liver. The radiologist says that they are worried about lymphoma. At this point, Molly is referred to an oncologist who performs an ultrasound guided fine needle aspirate of her liver and herpatic lymph node and confirms the diagnosis of lymphoma.

[00:48:03.05] Now when I first saw this case as an oncologist, seeing a case of hepatic lymphoma diagnosed preclinically when this dog has no clinical signs and not even any

changes on lab work was unheard of. I mean, these are patients that typically I see because they're very sick. They're not eating. They're losing weight. They're vomiting. They have markedly elevated liver enzymes and bilirubin. And their liver function is typically very poor.

[00:48:27.71] So we have to have a conversation about really, the health of the liver and trying to make sure that the liver returns to health so that we can get the cancer under control. So the conversation this oncologist is able to have with this family is very, very different. They have time to make the decision. They have multiple options to choose from in terms of what they want to do for Molly.

[00:48:50.45] And so, ultimately, they did go ahead and get her started on chemotherapy. And she's likely to do a lot better because she's starting from a place where she feels healthy. So just to review Molly's case, so this is a dog that has a family that asked for a way to screen for cancer because of a cancer signal detected and the confirmatory cancer evaluation that was performed.

[00:49:11.24] She was diagnosed with what's typically a very aggressive type of lymphoma but at a time where she was not yet clinically ill and she was able to go ahead and get therapy started, which means she's likely to do better by starting that therapy sooner. So my takeaways from this case is that there are these cancer warrior dog owners out there that are aware of cancer. They're asking for ways to screen for cancer. And they are absolutely relieved to have an option.

[00:49:37.46] In Molly's case, her cancer was able to be detected before she had any clinical signs. In a typically aggressive cancer, that often presents with organ failure. So this was caught much earlier in the process than most dogs with this specific type of cancer are detected. So she's likely to have a much better outcome. But we also know that one of the biggest prognostic factors in lymphoma is substage.

[00:49:59.25] So whether they're feeling healthy at the time of diagnosis, so this means that she's likely to do much better than if she had been diagnosed when she's feeling really poorly. So that's Little Miss Molly. Now that's kind of the screening use case. Let's look at aid-in-diagnosis as well. So that's the second kind of prediagnosis use case for OncoK9. And so this is really using this in dogs in which cancer is suspected.

[00:50:24.26] Some examples are listed on the screen here. So you might suspect cancer but it's in a tough place to get to inside of the body. And so the type of diagnostics to get there are really challenging to schedule, or perform, or risky, or that sort of thing. Or you might suspect cancer might be on your differential list but it's kind of nonspecific signs. And this can help to narrow down that differential list and help to guide, well, where do I go next, or the referral process, or things like that.

[00:50:53.76] Another use of it is, I think, nicely represented by Hank here. So Hank is a very handsome boxer mix that presented with a little bit of a low appetite. He was drinking a little

bit more, eating a little bit less. And his calcium was slightly elevated on his lab work. The veterinarian recommended to perform some thoracic radiographs. And we can see here that he has this mass in his cranial mediastinum just in front of his cardiac silhouette here, so cranial mediastinal mass.

[00:51:26.39] The veterinarian said, you know what? I'm pretty concerned. We've got some mild changes on lab work. He's got a few signs at home. But I see this mass. I'm very worried that he may have cancer. I think you should go for a referral. The owners were a little bit hesitant to go for immediate referral because Hank was feeling pretty good.

[00:51:44.61] And they said, well, isn't there something you can do? Can you get a diagnosis on this? Or can you do anything that's maybe noninvasive or doesn't involve referral? So the veterinarian said, well let's try this OncoK9 test. So they performed OncoK9. Now what happened in Hank's result is what we talked about earlier. So he not just got that cancer signal detected result but he also got this Cancer Signal Origin prediction of hematological malignancy.

[00:52:12.72] So now the veterinarian is able to go to the family and say, here's how Hank's feeling. I see this on X-rays. I see this on lab work. And now I have this result that is predicting that this is lymphoma. If you are going to go for a referral, you need to go right away. We need to get him in to see the oncologist. So at this point, he did go for referral right away.

[00:52:35.33] That was enough to convince them to go for immediate referral. And an ultrasound-guided fine needle aspirate was performed and confirmed a diagnosis of lymphoma. And Hank was able to go ahead and get started on therapy. So just by way of summary of Hank's case is that he had a cancer signal detected after cancer was suspected. And it also confirmed a CSO prediction.

[00:52:58.85] And this really helped the veterinarian convince the client to go for immediate referral so that Hank could get started on therapy before he got sicker. And he was able to get treatment started. Now finally, I want to just highlight that in some cancers like lymphoma, as I just showed you with Hank, detection rates are very high. But then we have these cancer types towards the right where the detection rates are lower.

[00:53:20.33] And it's helpful to just think through, when is the best use of the test? And that's highlighted well by little Shorty here. So Shorty came in for a wellness visit, had some dental disease, as well as this just adorable little mass at the base of his pinna. And the veterinarian recommended, I recommend a dental. I recommend to remove this mass. The owners wanted to think about when they wanted to schedule and asked if there was anything else that they could consider.

[00:53:48.32] The veterinarian had learned about OncoK9 and said, well, let's try this test. And so they went ahead and submitted OncoK9. Now, in the meantime, while they were waiting, which is about 10 to 11 days turnaround time for the results to come back, they

decided, in the meantime, to go forward with the dental and the tumor biopsy. And I received the results back, which showed a mast cell tumor.

[00:54:11.72] So imagine the veterinarian's surprise when they get this cancer signal not detected result. But this really just highlights that if you have these small cutaneous tumors, you can think about, there's going to be less biomarker around. False negatives can definitely occur with these small cutaneous tumors. And you're always going to be better served by direct tissue sampling, tissue biopsy rather than liquid biopsy.

[00:54:36.59] And when I just head on over to some questions, so I'm going to jump forward and just say that there are some advantages of this type of liquid biopsy testing. This is a simple blood draw, which your teams are used to performing, can be drawn in clinic the same day. You don't need to prepare these patients in any way. They don't need to be fasted. And everything that you need is included in a kit. So you don't need to run around looking for extra supplies to ship it.

[00:55:01.04] It covers multiple cancers. So it can detect 30 types of cancer. In some cases, a Cancer Signal Origin prediction can be made. And this has been validated in dogs with a wide variety of conditions. And those conditions are not likely to confuse this test. So there's very few false positives. And this is really cutting-edge technology. This is the same technology that the best human tests are using as well.

[00:55:24.48] And, I think, really, the holy grail of all of this is earlier detection, which can really help to shorten the path to diagnosis for our patients. And it might allow for earlier detection, maybe even prior to the onset of clinical signs as we've seen in some of these patients. And there's so many benefits. For us as veterinarians, we can offer more options for our patients. We don't have to be stuck in that situation that I was with Poppy where, I'm sorry, there's not a lot that we can do.

[00:55:50.12] If we can detect it earlier, we're going to be able to offer more options and also more time for them to make decisions if we're recognizing cancer when they're feeling good rather than when they're feeling very sick. This can really shorten the path of diagnosis, which can certainly save on finances. But really, the ultimate outcome is improved outcome and survival, hopefully for our patients by earlier detection. And that is really what is so exciting about all of this.

[00:56:17.13] So with that, I'll say a huge thank you. Please check out our resources page at petdx.com. And if you are watching tonight and interested in being a clinical study site, we always have ongoing clinical studies. So please send us an email. We would love to hear from you. And now I will turn it back over to Katie to see if we have any questions.

[00:56:37.44] Perfect. Thank you. We do have some questions. Can this test be used to detect cancer in cats?

[00:56:44.56] Oh, great question. So this test is species specific. So it does have to be matched to a canine genome, for example. So the test will not work for a cat. So don't send us 14 ml of your cat's blood, please. However, stay tuned because we really love cats. And we recognize that there are certainly clinical scenarios where this technology could be very beneficial for veterinarians managing feline care. So I would say, stay tuned for that. We're working on it.

[00:57:15.49] Very good. And what is the turnaround time to get results back?

[00:57:19.63] Yeah, turnaround time is-- it's about 10 to 11 days right now from the time that we receive it at the lab. And so that's calendar days.

[00:57:29.06] And what is the cost of the test?

[00:57:31.40] The cost of the test depends a little bit on where you're getting it. So again, it's available through PetDx. It's available through our diagnostic distributors like IDEXX and Antech. So reach out to them to ask, specifically ask your rep about the cost through those channels. But the cost to the vet is in about the high $300s. And most veterinarians are offering it for around $500. But again, that's decided at the clinic level. So totally up to the veterinarian in terms of what they charge for the test.

[00:58:00.33] Excellent. Is there any data that correlates earlier cancer detection with longer survival time in patients?

[00:58:08.91] Earlier cancer detection, yes, so that's a really great question. I want to see if I can pull up some slides. They just presented at the ACVIM Conference was last week in Austin. And I think that one important thing to think about is, when we think about early detection, there's two types of early detection. There's early stage detection, like detecting it at stage 1 rather than stage 4, for example.

[00:58:35.41] But there's also earlier clinical detection. And that's really where substage comes in. So if you think about detection prior to clinical signs, for example, we know, and these are going to look a little weird because these are ACVIM slides. But we know that there are many cancer types where earlier stage detection results in improved outcomes.

[00:58:54.13] This is not exhaustive. But these are just some of the studies that highlight improved prognosis for dogs that have earlier stage detection for the eight most common cancers. And then we have cancer types where we recognize that earlier stage detection results in better outcomes. So patients that don't yet have clinical signs, like substage A lymphoma does better.

[00:59:16.74] Hemangiosarcoma that's not yet ruptured does better, nasal tumors that are not causing a nosebleed, or brain tumors that are not causing seizures, mast cell tumors that are not causing ulceration or growing rapidly, and also, lung tumors that are not causing

coughing. So these are situations where it's not necessarily early stage. But it's early clinically in the course of their disease. And we know that there's many studies that highlight improved prognosis with earlier detection.

[00:59:47.67] Are you looking at prognostic and staging factors associated with cases where OncoK9 comes back negative?

[00:59:57.05] Are we looking at prognostic factors where it comes back negative? That's a great question. I would say that we have many samples from our clinical validation study that we're looking at the longitudinal evaluation of patients with many cancer types in the US over time. So yeah, we're looking at a lot of different prognostic factors because some of those are different by cancer type. And so we'll be looking at a lot of that when we look at those at the utility for those postdiagnosis use cases in evaluating in that situation.

[01:00:32.01] Is this test readily available in Canada right now?

[01:00:35.81] It is actually, yeah. So it is available from through Canada through all three of those channels. So I would say, you can reach out to our team at sales@petdx.com. Or you can also reach out to your IDEXX or Antech reps as well.

[01:00:50.85] Great. We have one last question. It looks like that is a case-specific one. What do you recommend the test for one of my recent cases? Seven-year-old lab, lame, painful in the left hip, had a squamous cell carcinoma removed from a toe of that same leg. X-rays showed bony changes of the left hip consistent with neoplasia and a large pulmonary mass, either primary or metastatic by a radiologist.

[01:01:19.05] I mean, I think that's a really good example of those aid-in-diagnosis cases, where both of those locations that you just mentioned. So a hip mass and a lung mass are locations within the body that are pretty difficult to get to when you're a general practice. So how do you get to those in terms of performing diagnostic sampling? And so especially because knowing what you're dealing with can be very important to making decisions about how to manage the case, or how to refer the case, or what the owner wants to do.

[01:01:55.44] I think that is a perfect use of the test to try to identify whether this is cancer or not. This a test that again is a qualitative answer. It's a yes/no. So it's likely to give you that answer of cancer, yes/no. But in terms of specific type of cancer, tissue diagnosis, tissue biopsy is always going to give you the most information. But if you can't get to those locations, this can be a good stepping stone, I think, in the diagnostic workup to help guide, where do I go next?

[01:02:32.68] Great. Well, thank you very much. I think that's all we have for tonight. I want to thank you for the presentation. And thank you, PetDx for sponsoring this webinar for everyone. It certainly was very informative. I know myself personally, I would love to be able to diagnose all the cancer diagnoses as early as possible to get that good outcome.

[01:02:49.54] I especially like ruptured hemangiosarcomas drove me crazy in practice. I love being able to get those early. So this is great information. And we'll go ahead and wrap it up. Thank you, guys.