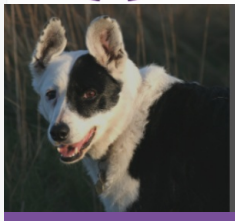
ONCOALESCE



Monograph

#3 October 2022

Greetings!

Dear Shah,

Treating Cancer; A new generation of climbing gear, and how to use it.

Welcome to the third edition of the Oncoalesce Monograph.

I apologize for the continuation of the poorly shoe-horned climbing reference, but it is still applicable and as an (increasingly ex-) climber, I like it!

This edition has some very new information for you - Multi-center CAR T-cell clinical trials, an introduction to a new oncolytic virus, a new surgical pain relief medication for cats (yes, something new for cats) and genomics to treat melanoma. The Oncoalesce Monograph also helps you understand how these new technologies can be incorporated into general practice.

As one panel member reported "Some of the data and stats would go over my head, so how can we help implement these things in the clinical setting. This project helps to understand the practical side and to gain the tools to bring these things into the discussion.There are lots of problems with working on new approaches, with a heavy work load, trying to change the discussion, changing the administration so they adopt new things; these are all difficult and Oncoalesce will help with this".

I hope so...

Tariq

PS - if you are heading to Norfolk, safe travels and see you there.

Email me!

Disclaimer and stuff

The following notes have been taken directly from data presented to the panel of oncologists in the Oncoalesce meeting #3. They then contain direct quotes and questions from the panel as well as the answers provided to them by the companies.

It is important to note some views presented here are made by individual oncologists but are not necessarily representative of the whole group. Whilst the panel comments are direct quotes, they are anonymized.

Conflict of Interest: All members of the panel were paid for their time by Oncoalesce at an industry acceptable hourly rate. They were not paid any other monies and act independently from the companies represented.

Panel:

- Dr. Jeff Bryan - University of Missouri
- Dr. Kim Cronin - MA Veterinary referral hospital
- Dr. Pamela Jones - QBiotics
- Dr. Kendra Lyons - In-between
- Dr. Melissa Parsons-Doherty – Pearland Animal Cancer and Referral Center
- Dr. Erin Roof – Animal Cancer Care Clinic
- Dr. Aarti Sabhlok – Ethos Pet Emergency and Specialty Ctr Marin
- Dr. Andrew Vaughan – Las Vegas Veterinary Specialty Center
- Dr. Rachel Venable - Pet Cancer Care Consulting
- Dr. Carissa Wood - TOC Oncology

Companies
- Elias Animal Health
- ImpriMed
- Canine Biologics
- Elanco
- Vidium Animal Health
- Jaguar Animal Health
- Nutramax

There are at least 24 companies with an active presence within veterinary oncology. I hope over time more companies will be represented through Oncoalesce and will use this platform to provide clinically relevant information for you to be able to trust and adopt.

LEAH
LABORATORIES

Launching the first gene edited cell therapy for dogs

LEAH Labs is building living cell therapies to help dogs with devastating diseases. We are focused on bringing Chimeric Antigen Receptor (CAR)-T cell therapy to dogs that have B cell lymphoma. LEAH Labs was founded in late 2018 to be the first company to bring this technology to pets, and we are launching our first pilot trials for dog patients.

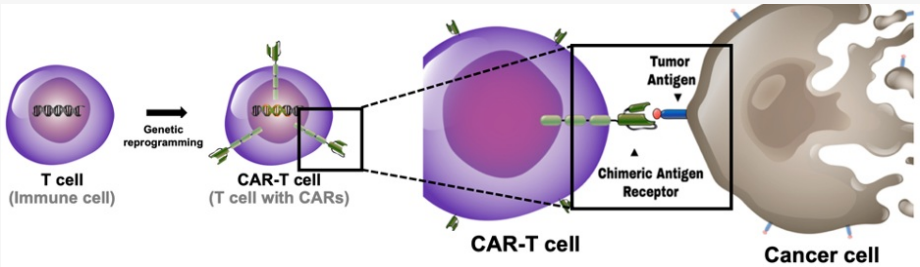
CAR-T cell therapy is a breakthrough technology that reprograms living immune cells so they can seek out and destroy cancer. There are now six different CAR-T cell therapies that are FDA approved for multiple cancers and cancer subtypes in humans.

How does CAR-T cell therapy work?

Uniquely, LEAH Labs is building a platform that allows the use of human T cells in dog patients. Specifically, we use CRISPR technology to make genetic mutations in the “T cell receptor alpha” gene, disrupting its expression on all cells used in our therapy. This is vital in eliminating the potential for these human T cells to cause Graft vs Host Disease (GvHD). Because of our innovative gene editing platform, we can engineer multiple doses of CAR-T cell therapy in one manufacturing run. Currently, we use lentivirus to deliver the genetic information encoding the CAR into the T cell genome.

We are enrolling our first pilot study at Minnesota and Missouri, with Ohio State coming online soon.We aim to build a data package for the safety and efficacy of our first product. This a fully funded and stipend-compensated study. All dogs 15kg-50kg (except boxers) are eligible for enrollment. The core study lasts 21 days, at which point dogs will be reassessed for progression (and coming off the study) or stable disease/remission (and continuing on with data collection). For a full description of enrollment criteria and to refer one of your patients for this study, please visit the links below.

Questions or comments? Please message our CEO, Dr. Wes Wierson, at wes@leahlabs.com



Enrollment page at University of Minnesota

Enrollment page at University of Missouri

The Discussions

vidium ANIMAL HEALTH a TGen subsidiary

A Deep Dive of Mutations in Canine Melanoma From the Literature

There is already a lot of information in the primary canine literature reporting mutation-level evidence. We found a total of 19 peer-reviewed papers, published from 2004 all the way to this year that describe the mutations found in canine melanoma. We have divided these 19 studies based on study types, which are either candidate gene approaches (e.g. PCR or Sanger sequencing) or genomic approaches (e.g. whole-genome sequencing, whole-exome sequencing, or targeted panel sequencing, which is what SearchLight DNA is). The targeted sequencing approach has been frequently utilized in the clinical setting due to its cost effectiveness, quick turn-around time, and high diagnostic utility.

From these 19 studies, 11 of them, corresponding to 418 samples, were analyzed by candidate gene approaches, and 8 studies comprising 220 cases were profiled by genomic approaches. So, our vet community has the documented mutation status for over 600 canine melanoma cases via these *published* studies.

SearchLight DNA Melanoma Cohort

There have been 66 melanoma cases that Vidium has sequenced, primarily from the oral cavity(86%). In 97%, mutations were identified with diagnostic, prognosis, and/or therapeutic associations. We've identified 84 commonly mutated genes in our melanoma cohort, including prognostic biomarkers that are associated with unfavorable clinical outcomes, along with therapeutic biomarkers in 81% of cases with associated sensitivity to several targeted therapies available in veterinary compounding pharmacies.

Summary

- There is a lot of clinical actionability in the mutations that we find in the majority of canine melanoma cases.
- SearchLight DNA is based on curated peer-reviewed, published literature with high evidence levels
- SearchLight DNA covers many genes and mutation types AND accepts ASPIRATES

SearchLight DNA Review

- SearchLight DNA utilizes Next Generation Sequencing (or NGS) to look for several mutation types, including single nucleotide variants, indels, copy number variants, and internal tandem duplications. We cover 120 important cancer genes.
- SearchLight DNA is a targeted sequencing panel that is undergirded by our biomarker database, Vidium Insight. Vidium Insight is where we've curated every PUBLICATION that's ever been described in a mutation in canine cancer, and we've also lifted over from the human space using "caninization" of the human data, where we lift their mutations into the canine equivalent, using translated protein alignments and conservation scoring, to try to infer from human data. We use a rigorous process to bring in human data, which focuses on the inclusion of biomarker associations with the highest evidence levels from human oncology.
- FFPE slides and paraffin blocks are preferentially requested from reference laboratories so that we can have the option of macrodissection, which will boost tumor content to exceed the minimum threshold based on our validation studies and therefore be able to confidently report our findings. But, we don't always get what we request, which is the advantage that we have by having our own Specialty Pathology Service right under the same roof. If the sample is already with us to begin with, we can macrodissect if needed.

SearchLight DNA Clinical Utility

- The best way to think about the clinical utility of SearchLight DNA is as a triad of diagnostic, prognostic, and therapeutic information.
- SearchLight DNA can be used for ANY cancer case for which you or the pet parent may want more information.
- Keep SearchLight DNA in mind if you have poorly differentiated tumors that are difficult to diagnose, despite other diagnostic tests you may have performed, like IHC or PARR.

Vidium report that hey have received many comments from oncologists that they were unable to order drugs direct from Wedgewood unless they were part of a drug program. **This is not the case**, and all targeted drugs are available from Wedgewood on-line. Other pharmacies do offer many of these drugs e.g. Stokes or BestPet Rx

How much do we know about some of these drugs being recommended? There were some provided in the presentation that I had not heard of before?

The reports do recommend drugs we have much information on e.g. Olaparib or Lapatinib, but there are other drugs from the human side that we know less of, and

even drugs drawn from human data that we do not yet have access to through compounding pharmacies e.g. Niraparib, Rucabarib or Talazoparib. There are included because the evidence in the literature is high enough to warrant inclusion based on our logic. It is the hope that over time we can establish tolerability and then see how they compare to SOC. For the ones we have access to, but know less about – we still have data available including canine specific data like toxicology and PK data from the NDA reports and this is provided in the drug monographs available to oncologists. The monographs also contain sourcing and pricing information for the drugs. (link below for Monographs from the Vidium website).

Why is Melanoma being presented?

The data had already been pulled together for a series of webinars which will also be available online, as well as melanoma being one of the big hitters that we see, that has a high level of actionability.

It is good to see some of the methodology behind the development of this assay, the choice of mutations and why you focus on certain genes. This is useful to understand as other parties (e.g. the hospital pathologists) are asking questions about this technology.

This is a useful tool because it also provides good diagnostic and prognostic information, regardless of whether or not you can get a therapy out of it, you can still gather more information about the cancer. Running it on cytology makes it more useful.

Link to drug Monographs

Client education in CID

There are many moving parts to achieving a successful medical outcome in treating CID, and actively engaging with the pet owner is a critical part. This presentation dicussed the owner education available from Jaguar Animal Health.

Chemotherapy is both a medical and quality of life issue for the pet and their family and CID can be a treatment limiting side effect. Severity of diarrhea is often very subjective and the dog owner experience is not based purely on clinical severity. Client education on managing side effects can help the client experience and improve compliance and satisfaction.

There is a patient trifold available from the company addressing many of the key questions, saving you and your staff valuable time. The hand-out also deals with the botanical source of Canalevia, sustainably harvested as a natural remedy. There is also a link below to the information on their website (further saving actual trees being chopped down and made into paper :-)

For some clients this is really important information, but some clients are not bothered…, but certainly there are those around here (Oncologist in California) who would appreciate the fact that it is a botanical, sustainably harvested drug. This would be a big selling point compared to using traditional antibiotics like metronidazole.

Can clients get it elsewhere?

It is not available easily e.g. from Chewy, but there is home delivery from distributors (Question the speed of this delivery? Or fees? But then there are no markup issues?)

I've used it twice – cost is not an issue; people just want the diarrhea resolved and anyway we are leading the way in oncology and trying new products.

It did not work in my cases, but these were heavily refractory cases with chronic diarrhea.

It is indicated for acute diarrhea and is not a long-term therapy therefore we would expect a lower response rate than 75%.

Clients who have been prescribed metronidazole in the past may be unhappy with the price increase.

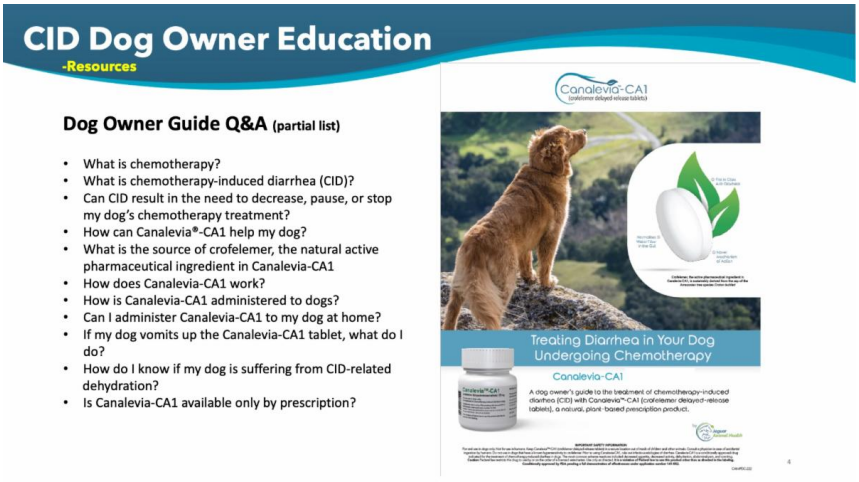
Yes, but this does not affect new clients!

It can be a hard one to sell to management, especially since there isn't a clear need for the product?

(Another panelist reply) : Yes, it may be at times, but look at the science, it has a

direct indication, it has a license! I know it is not chemotherapy for cancer but a treatment for diarrhea, it will take time but we will get there.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Use only as directed. **It is a violation of Federal law to use this product other than as directed in the labeling . Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-552.**



Link to Owner information

Avmaquin™

Sulforaphane Producing Supplement

nutramax LABORATORIES VETERINARY SCIENCES, INC.

Sulforaphane and its role in Canine cancer, specifically TCC

Sulforaphane (SFN)is produced from the interaction of Glucoraphanin and Myrosinase in cruciferous vegetables, notably broccoli. However, levels are variable hence a concentrated supplement containing these precursors is the most reliable and consistent source of sulforaphane.

At the cellular level, SFN activates Nrf2, a transcription factor which increases the gene expression of phase II detoxifying and anti-oxidative enzymes.
Initial PK/PD work in beagles with an oral SFN source demonstrated a once daily administration gave significant SFN plasma levels and resulted in an increase expression of NQ01 gene activity (a key gene in the detoxification/antioxidant process). They also saw increased concentration of SFN in urine.

In a comparison of two published studies, plasma SFN concentrations achieved with Avmaquin was seen to be considerably higher compared to a similar product Broccomax.

Avmaquin also contains beta-glucans which works synergistically with SFN demonstrated by measuring NQ01 gene expression.

In vitro and rodent studies demonstrate SFN to be a potent inhibitor of carcinogenesis, targets bladder carcinoma and can suppress bladder cancer progression by inhibiting the expression of FAT atypical cadherin 1 whose expression is shown to be increased in bladder cancer cells.

Studies using laboratory animals treated with doxorubicin demonstrated that sulforaphane can protect cardiac muscle cells (myocytes), decreasing cardiac mortality by 85-90%. The studies also showed an increased tumor sensitivity to doxorubicin. Results also indicated that doxorubicin administration could be reduced up to 50% when used in conjunction with sulforaphane. Additional studies utilizing other chemo agents showed the prevention of cisplatin-induced nephron inflammation and tubular cell death in the kidneys.

Presently, one controlled human breast cancer clinical trial is in progress assessing the cardioprotective benefit of sulforaphane in humans treated with doxorubicin

It is great to see bioavailability data. Next steps should be to try and quantify protective levels of gene expression e.g. NQ01, and general biologically effective doses of Avmaquin.

Nutramax agreed and explained they have planned further in vitro work as well as clinical trials (already begun) to help support these claims

So, should we be giving Avmoquin to dogs with existing bladder cancer to prevent/slow down additional progression of the disease in addition to prednisone treatment?

Yes, we have enough published and experimental data as well as anecdotal open label cases of such dogs to demonstrate efficacy in terms of lowering or stabilizing BRAF levels, and Avmaquin should be considered if standard of care is turned down.

What about concurrent use with chemotherapy, especially since it has antioxidative properties

We don't know absolutely the antioxidative properties of SFN, whilst simultaneously increasing sensitivity to doxorubicin which causes oxidative damage. There is clearly a balance there somewhere.
Human data so far does not suggest a contraindication when using Avmaquin with palliative treatments e.g. NSAIDS in TCC treatment, but there should be some caution when using with chemotherapy until we understand more.

What is the role of Avmaquin especially as an anti-inflammatory, in preventing or treating haemorrhagic cystitis?

This is an interesting question, and this would be a good indication that the company intends to pursue. It is potentially efficacious in this scenario.

Email me if you would like some free samples for your hospital to trial

ELIAS®
ANIMAL HEALTH

ELI352 – An Oncolytic Virotherapy for Cancer in Veterinary Patients

Elias is focused on immunotherapies and adjunct therapies that can work alone or can be combined with ECI® or other therapeutics as needed. Elias presented a sneak preview of a new product that is under development

Introduction

Many oncolytic viruses are being evaluated as cancer therapeutics in both humans and canines. ELI352 is an oncolytic virotherapy being developed as a cancer therapeutic for canine malignancies. An oncolytic virus is a virus that preferentially infects cancer cells causing oncolysis (death) of the cancer cell without causing excessive damage to the surrounding normal tissue. This disruption of the cancer microenvironment can induce or boost an anticancer immune response. These viruses have the potential to be used in combination with other immunotherapies such as adoptive T cell therapies or checkpoints and/or with traditional therapies such as radiation and chemotherapy to improve outcomes.

ELI352 was isolated from a wild type stock of the Lister strain of vaccinia virus. This specific virus is not genetically modified. It can be safely administered intravenously as well as intratumorally. ELI352 has demonstrated *in vitro* activity against 4 separate canine cancer cell types – soft tissue sarcoma, melanoma, osteosarcoma and prostate carcinoma. Cancer cell death was demonstrated in all four cancers, both at a virus to cancer cell ratio of 1:1 and 0.1:1 ratio. The best efficacy was seen against melanoma cells.

Dose escalation study.

11 dogs diagnosed with cancer were intravenously dosed with ELI352 once weekly for 4 weeks. One dog in Cohort 2 received a total of 7 weekly administrations. Due to efficacy observed after its initial four infusions an additional three doses were administered. There were no dose limiting toxicities noted in that study with the highest dose being 3x10^9 plaque forming units per 25kg of body weight. The maximum tolerated dose was not achieved.

There were 8 drug related adverse events from mild to serious, with one life threatening adverse event reported as acute tumor lysis syndrome in one dog with a solid tumor. The patient did recover.

Circulating tumor cells (CTCs) were also evaluated as an additional efficacy surrogate. CTCs are tumor cells that have sloughed off from the primary tumor and extravasate into the circulation. Canines treated with ELI352 showed a significant reduction in circulating tumor cells from baseline screening levels and the figures show, some of those reductions were quite significant and sustained.

Peripheral blood samples were collected at baseline, week 2, week 4, and week 8 for evaluation of CD8 positive T cells, CD8 positive T regs, and myeloid derived

suppressor cells (MDSCs). There was a significant reduction seen in some immunosuppressive cells. MDSC cells are significantly reduced while CD8 positive T cells significantly increased. In evaluating the potential immunostimulatory effects, the investigators looked at the ratio of the CD8 positive T cells relative to their immunosuppressive cell populations. The ratio increases significantly where peak effects were noted about 4 weeks after treatment indicating a potential immunostimulatory signal being seen post oncolytic viral therapy.

Although this dose escalation study was not primarily looking for efficacy, RECIST measurements of tumors were assessed via CT scan. Two partial responses were noted, one in a mast cell tumor patient and the other in a T-cell lymphoma patient. It is worth noting here that patients will develop neutralizing antibodies to the virus fairly quickly, causing a small therapeutic window of efficacy lasting a few weeks if used as monotherapy.

Oncolytic virus therapies are most likely to be used in combination therapy to improve outcomes in treating canine and human malignancies. Their ability to disrupt the cancer microenvironment can potentially trigger immune activation and improve the efficacy of other immunotherapies such as T cell therapies or checkpoints. In addition, there is an increasing body of evidence and research that oncolytic viruses, as an adjunct to chemotherapy, can significantly improve outcomes.
Finally, oncolytic viruses such as ELI352 can potentially turn chemotherapy resistant tumors, “cold” ones, into chemotherapy susceptible “hot” ones through the disruption of the tumor microenvironment. For example, ELI352’s sister *vaccinia* strain (called Olvi- Vec) has demonstrated this in human clinical trials treating platinum-resistant/ refractory ovarian cancer.

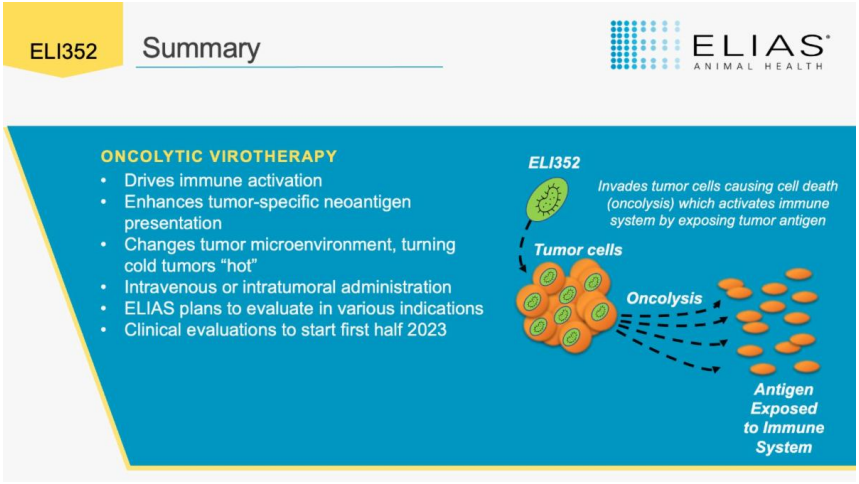
Clinical evaluation of ELI325 is due to start early 2023.

The Panel expressed concerns over the safety of the virus

This is a wild strain non-pathogen virus that is unable to cause disease.

“It would be fabulous to use this in refractory cases, to re-prime or reset it; maybe in melanomas?

That is the plan; on the human side they are launching a phase 3 trial in platinum resistant ovarian cancer.



Link to human trial - platinum resistant ovarian cancer (Int. J. Gynecological cancer)

CANINE BIOLOGICS

Metabolic & Nutritional Considerations for Dogs with Cancer

Dr. Korinn Saker, DVM, PhD, Professor of Clinical Nutrition
NC State University College of Veterinary Medicine

Dr Saker recently did a presentation about cancer diets for the university’s oncology department. She explained that understanding what happens to the nutrients in a cancer patient is important to ensure they are getting fed appropriately both in terms of delivering the calories they need as well as developing a formulation that helps slow tumor growth and decrease the side effects of the cancer. Dr. Saker reviewed tumor cell survival skills and explores how healthy cells and tumor cells differ in carbohydrate metabolism and how this impacts the metabolic and nutritional needs of dogs.

The following is a summary of the presentation.
For a full transcript please follow the link below.

Energy (ATP) production
Tumor cells decrease differentiation of certain host cells so they end up having altered homeostasis.
Tumor cells also secrete a variety of cachexia-promoting compounds that hasten malnourishment. The tumor cells promote metabolic inefficiency in host cells by encouraging the production of lactate from pyruvate rather than the pyruvate entering into the Krebs cycle, whilst they themselves have an ability to increase uptake of glucose compared to a normal cell. The host cell utilizes the lactate for energy, but in an inefficient way (Cori cycle) causing a negative energy balance. Finally tumor cells increase their energy production from anaerobic glycolysis due to having less mitochondria. The Canine Biologic formulation is a low carbohydrate diet to offset this imbalance.

Lean Body Mass
Lean body mass is the predominant source of protein in the body. If it is not adequate in the diet, the body starts breaking down lean muscle mass to get the protein it needs. Malnutrition and cachexia are a major cause of lean muscle mass loss. Proteolysis is enhanced in tumor cells. These cells act as a nitrogen sink and trap amino acids and utilize them for energy through oxidation and for protein synthesis to get the proteins they need for their proliferation. There is a constant battle over whether healthy cells or tumor cells are going to get the protein and carbohydrate and which is going to get first use after a meal.
For this reason the formulation has an increased protein component.

Tumor cells can up-regulate the UPP pathway allowing it to alter the shape of the protein making it unusable by the host. However, the UPP pathway can be interrupted or regulated by increasing the EPA in the diet. Aside from being anti-inflammatory, omega-3 fatty acids have been shown to be anti- tumorigenic and anti-cachectic. Altering the UPP pathway is one way this happens.
Using an EPA-rich diet can help preserve lean body mass and muscle mass in oncology patients.

The ability to modulate the fat in the Canine Biologics diet allows clinicians to help patients with comorbidities, e.g. pancreatitis.

This information is very important and used to be taught, and at the time we had Hills ND. Maybe we are rediscovering this now and we need to provide it in a palatable form for owners. What is the difference between Canine Biologics and ND?
ND had far higher (and inflexible) levels of fat, causing a very high incidence of diarrhea. CB does not have this. It is also a more nutritious diet based on the method of production and quality of ingredients. Being freeze dried it becomes far more palatable than ND.

A non-chicken formulation is being developed containing beef. A range of the supplement mix is also being tailored to specific groups of cancer.
Shelf life is 2-3 years, though the food component itself lasts far longer (The manufacturing plant they use also prepares camping food).

CB are also going to launch a line of complimentary treats, keeping the same formulation and the same good healthy balance.

For many clients food is their biggest focus, and often it is our smallest focus and the thing we want to spend the least time on. There is for sure room to grow and learn and be better at what we do regarding nutrition. It will require a philosophical shift for oncologists to spend more time discussing diet as part of a holistic approach. I think the idea of the company offering treats is a big deal and they cannot get them out fast enough.

If clients can get hold of these treats, it would be the best form of advertising for them.

Nutrition is an important component for our clients and I just don't have enough time to discuss this – we should be doing more.

One client wanted so much information – I sent them to the company; they spent 45 minutes on the phone talking about food and diet so I didn't have to! They are nice and help, which is great.

Full transcript of Dr. Saker's talk

Zorbium™ - Buprenorphine transdermal solution

Zorbium is an Opiod - Important Safety Information: Before using Zorbium, read the accompanying prescribing information including the boxed human warning

Dr. Todd Duffy presented a brief introduction to Zorbium; Elanco's new buprenorphine transdermal solution delivering a single topical dose to provide post operative pain relief for cats for a four-day duration.

Presentation is 2 pre-dosed tubes for simplified application and record keeping. Smaller cats (2.6 - 6.6lbs) = 8mg (0.4ml). Larger cats (6.6 – 16.5lbs) = 20mg (1ml). The solution rapidly dries within 30 minutes after topical application forming a depot within the skin that releases buprenorphine continuously into systemic circulation. The benefit of Zorbium is that it reduces the challenges of administering pain medication at home and helps limit the risk of opioid misuse by pet owners. Zorbium should be applied 1-2 hours before surgery.

In a safety and efficacy trial it was determined that 81% of cats treated with Zorbium were considered a treatment success vs 40% in the vehicle control group. AE's were minor, with hyperthermia being significantly different between the two groups post-operatively.

For full details of Zorbium, please refer directly to Elanco Animal Health

Does this have a role in medical oncology – is it more for surgical or radiation oncology?

There was a general agreement that this has a place for all 3 divisions with so many reasons for use.
If you are using buprenorphine for multiple days at a time, then Zorbium could satisfy this need. Cats with oral SCC, and other oral tumors would benefit.

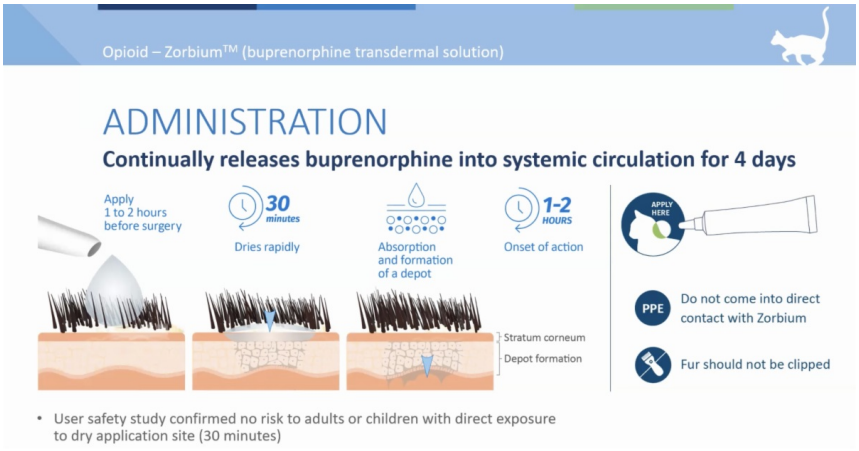
Dr. Duffy added: The safety study was a 4-day trial, so there is little data for subsequent days. The data suggested there may be some stacking phenomenon when you have residual product from a previous dose so one should be mindful of this. There are many variables that can affect this. A solution may be to provide the human formulations for owners to offer if necessary, then Zorbium could be reapplied once the pet returns to the hospital.

Cats with oral SCC, and other oral tumors would benefit.

None of the panel have used Zorbium yet but given its applicability there was agreement that oncology should know about this product. Members of the panel reported that they would be stocking it from now on.

It would be of use in palliative care – the "fentanyl patch for cats" – there is a definite place for this, especially in the oral squames and is considerably better than orally medicating a cat whilst ensuring they have the pain medication they deserve. It could help in getting them ready for radiation also.

So many people can't medicate their cats with anything orally, it scares me when I send them home with 5ml of buprenorphine (prepared by a compounding pharmacy so they can do the checks) – this is so much nicer because they can't abuse it – it makes it considerably easier this way.



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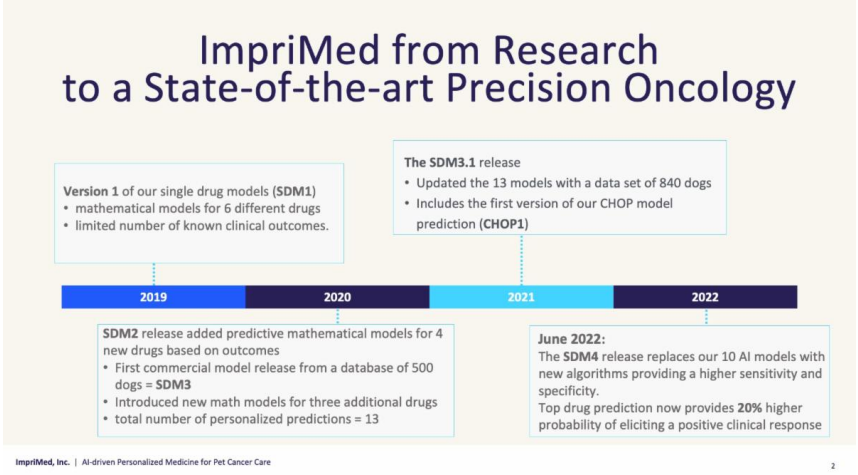


ImpriMed from research to State-of-the-art precision oncology

Artificial Intelligence learns from systems and data, so the more clinical and patient information received, the better the AI and machine learning works. This process is streamlined using the vet portal for easy entry of information. The original assay has progressed through 4 iterations (see timeline above) since the initial launch, which immediately addresses the experience "I used it once before – it didn't work…."

Imprimed presented data to attempt to allay some of the questions and concerns from oncologists.

Q: "The ability to predict a B cell lymphoma's response to CHOP [with ImpriMed] was not significantly different from the data that is available from the literature based on immunophenotyping, so it does not appear as though there is a clear advantage to using it. I would consider this to be better looking at T cell forms of lymphoma and atypical presentations of lymphoma where it is harder to decide what to use and that CHOP is still often used as the default."

(Slide 1 below)
Among the 3,000+ patients who requested ImpriMed services, about 600 patients received the CHOP prediction reports so far. The likelihood of CR and the likelihood of relapse for a CHOP protocol were different for each patient regardless of the patient's immunophenotype (B or T), which confirms that we need a personalized approach even for CHOP protocols. The data just gives you an average based on a small population. This assay is tailored specifically to the patient.

Q: "I still think the greatest utility of this assay is for atypical presentations (aberrant immunophenotypes, unusual organ involvement, etc.) or relapsed patients."

(Slide 2 below)
Yes, we provide great value to atypical or relapsed patients. However, most of our serviced patients are naive lymphoma patients. Our users provided highly positive feedback on patient-specific comprehensive information for naive lymphoma patients, which includes single & CHOP drug response predictions, PARR, and flow cytometry altogether.
Based on our predictions ImpriMed works for both naïve and relapse cases; we intend to present more data at our next meeting on relapse cases for your review.

For naïve patients:
- Drug response predictions can be a good starting point for new patients
- To quickly identify potential CHOP failure patients (non-responders)
- To predict best single-agent therapy
- To predict treatment options for patients with comorbidities or contraindications

For relapse patients:
- To predict when 2nd line CHOP will start to fail patients
- To help identify drug resistant cases (changes since last assay or treatments)
- To predict best single-agent therapy options or additions to other protocols
- To identify changes over time

Q: "I would like to see more of the flow cytometry data that has been generated particularly the less common subtypes of B and T cell forms of lymphoma. I think that this data would provide a stronger argument for using this type of an assay. "

(Slide 3 below)
We've provided our flow cytometry results to 2,300+ canine hematologic cancer patients, and we were able to cover less common immune subtypes as shown in the following table: Almost every sub-type has been assessed in our lab and optimized with real-world clinical outcomes. We recently updated our sensitivity and specificity for PARR and will share once approved.

Q: "My biggest concern remains that nobody has made this work on the human side. It leaves me skeptical that chemosensitivity prediction will ever be valid in dogs or cats."

ImpriMed is not just a chemosensitivity assay company! We optimize patient's clinical outcomes by using AI. Cell-based functional precision medicine approaches are being highlighted more and more in human medicine. In the human oncology space, there are several functional precision medicine companies or example Xilis, Notable Labs, and Cellworks.

The chemosensitivity assay result is only a part of various data points for our AI models. For each lymphoma patient we combine multiple parameters from live cell-based drug sensitivity tests, immunophenotyping assays (PARR and flow cytometry), blood work, and the patient's signalment. Models are continuously trained on real-world clinical outcome data to predict personalized drug responses with increasing accuracy from comprehensive information about patients and their tumors.

ImpriMed recently partnered with Mayo Clinic to help develop and validate their AI-driven personalized medicine platform for human blood cancers!
See link to press release below.

Panel:
I've used Imprimed several times since the last meeting, especially on naïve patients rather than just relapsed. Most are B-cells and the CHOP prediction model suggests a great response. I am struggling with one that gave a poor prediction and am still deciding what to do with it. I had another case that had a poor CHOP prediction, with a very low prediction for Doxorubicin. However, the mitoxantrone was very high so I have substituted these two and time will tell.

This is a common problem in the early days. ImpriMed is a tool to provide you with as much information as possible so you begin with a more educated idea of how to handle these patients, but we can't tell you specifically what protocol to use. With , experience, oncologists will be able to act more confidently on the prediction report information and change what they do.

If you run the assay and it provides a poor prediction but you choose to go ahead anyway, if/when the patient relapses early and you use the report for plan B – is it still valid, or will the tumor have changed at this point and should you do a second test?

This is common as old habits die hard and oncologists do go ahead with what they are used to. You can use the original report for plan B if it is very early, but it is better to run a second assay; even after a month we see some large changes in response predictions. More data on serial assays will be presented next time. It is worth noting that a second assay on the same patient is half-price.

Are you still working on this for cats?

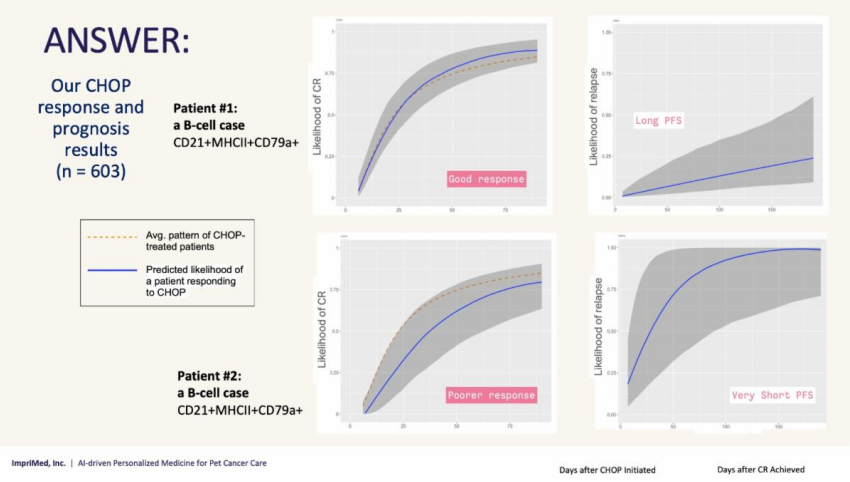
Yes, and we are still providing free flow and PARR for feline samples so please send them in.

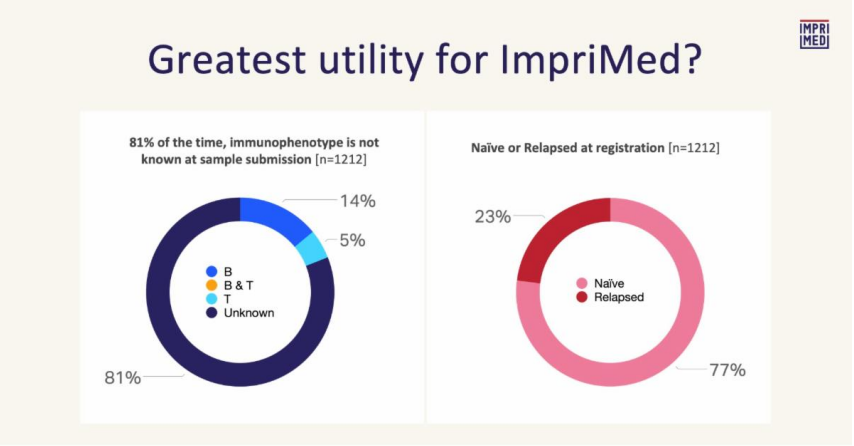
We've just got approval at our hospital for ImpriMed, but there is some push back on long term data and whether or not it changes patient outcome in the long run. What are your plans for addressing this?

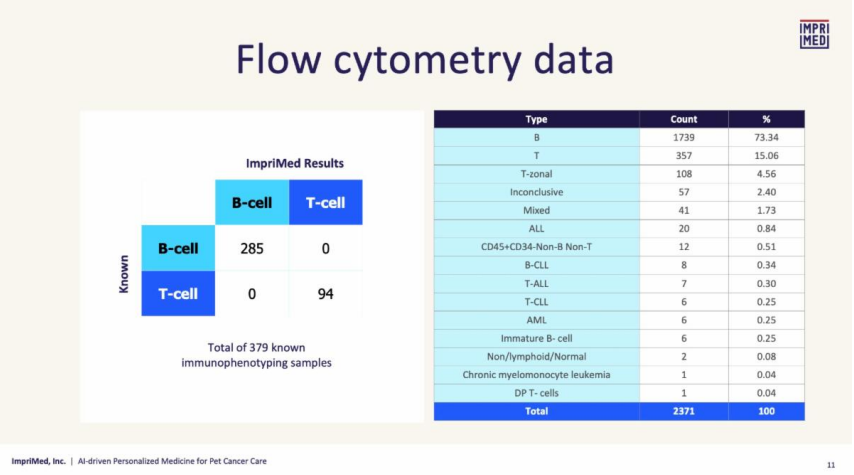
We do have some progression free data in the last published paper. As we finish this round of funding we have a plan in place for a trial comparing the clinicians choice vs the ImpriMed report.

We should be offering something more than just CHOP; we should put the best protocol first and I discuss Imprimed in this light – This may be a way we can modify the standard protocol to improve outcomes.

I am trying to use this more in naïve patients, I have used their predicted individual drugs predictions where the CHOP prediction did not look good, and some of my cases have done very well. It would be great at some point to see some survival data. [Yes – that would be brilliant and I hope we have this in time]







Type	Count	%
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T-zonal	108	4.56
Inconclusive	57	2.40
Mixed	41	1.73
ALL	20	0.84
CD45+CD34-Non-B Non-T	12	0.51
B-CLL	8	0.34
T-ALL	7	0.30
T-CLL	6	0.25
AML	6	0.25
Immature B- cell	6	0.25
Non/lymphoid/Normal	2	0.08
Chronic myelomonocyte leukemia	1	0.04
DP T- cells	1	0.04
Total	**2371**	**100**

Link to more information on the partnership with the Mayo Clinic

COMO Pride, with Isabella.

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