

ONCOALESCE



Monograph

#7 July 2023 (Part 2)

Greetings!

Dear Shah,

Welcome to part 2 of "July's Oncoalesce #7" You can download previous versions following the link below. The audio versions will also be available through this link (Part 1 is now available).

I hope those of you interested in exploring the possibilities of ECT appreciated the suggested protocol from LifePulse Bio.

This week we are taking a break from pure science and looking at the environmental background to Jaguar Animal Health and Canalevia-CA1. Clients appreciate the message of sustainably harvesting natural products and supporting the local environment and they will find the Amazonian background to Canalevia very interesting. It is a good story. There are also

some good clarification points to its mode of action in "secretory diarrhea".

Enjoy,

Tariq

Email me!

Download PDFs of this and previous editions

Disclaimer and stuff

The following notes have been taken directly from data presented to the panel of oncologists in the Oncoalesce meeting #7. 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.

I am a paid consultant for the 6 companies represented in these monographs through Oncologize but I do not receive extra fees for publishing the Oncoalesce Monographs or for any content herein.

- Panel (not all are present at every meeting):
 Dr. Jeff Bryan University of Missouri
 Dr. Kim Cronin MA Animal Cancer Care Specialists

- Dr. Pamela Jones QBiotics
 Dr. Kendra Lyons Locum
 Dr. Melissa Parsons-Doherty Pearland Animal Cancer and Referral Center
 Dr. Erin Roof FL Animal Cancer Care Clinic
 Dr. Aarti Sabhlok San Francisco Animal Medical Center.
 Dr. Pachel Venelle, Pet Cancer Care Consulting

- Dr. Rachel Venable Pet Cancer Care Consulting Dr. Carissa Wood FL Animal Cancer Care Clinic
- Dr. Rachel Kovac TX Animal Diagnostic Clinic

Companies

- Elias Animal Health
- ImpriMed
- Vidium Animal Health
- Jaguar Animal Health Nutramax Laboratories
- LifePulse Bio
- Hills

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

The Discussions







Extracting sap from a Croton lechleri tree in the Northwestern Amazon

Canalevia-CA1 is a FDA conditionally approved product to treat chemotherapyinduced diarrhea (CID) in dogs. Currently, treatment for this condition is not adequately addressed by other available medications.

Canalevia-CA1 fills a gap in available treatment options, easing the burden of illness and providing a well-tolerated treatment for CID in dogs. Canalevia-CA1 has a novel mechanism of action that normalizes the fluid influx into the intestinal lumen that can improve the quality of life for the dog.

Canalevia-CA1 is now available through Stokes pharmacy who offer a 24 hour service. This allows you to prescribe Canalevia-CA1 even if you don't currently stock it. If you do stock it, you have the option of providing all chemotherapy cases with 2 tablets of Canalevia-CA1to keep on the shelf as a just in case. If they do suffer from acute diarrhea, they can begin treatment immediately and order the remaining course of 4 tablets direct from Stokes.

What is the source of crofelemer, the natural active pharmaceutical ingredient in Canalevia-CA1?

The term ethnobotanical refers to the use of plants by Indigenous people in their everyday lives, including the use of plants for medicine. Crofelemer, the active pharmaceutical ingredient in Canalevia-CA1, is a natural product sustainably derived from the sap, or latex of the Amazonian tree species *Croton lechleri*, which has a rich history of medicinal use by Indigenous peoples in the Western Amazon rainforests of South America.

The tree produces a blood-red latex from which crofelemer is isolated and purified. The latex of the *Croton lechleri* tree is commonly called "Sangre de drago" in Spanish, which translates to "Dragon's blood". Because the tree's latex is one of the most widely used plant-derived medicines in the western hemisphere, extensive research has been conducted on the chemistry and pharmacology of *Croton lechleri* latex. The latex continues to be part of rural and urban traditional medicine in multiple countries, including Peru, Ecuador, and Bolivia. Traditional Indigenous healers have utilized the latex for centuries as an oral treatment for a variety of medical conditions including diarrhea, stomach ulcers, coughs, and flu and they apply the latex topically as a wound-healing agent for cuts, open sores, and for healing the gums after tooth extractions.

A Longstanding Commitment to Benefit Sharing & Sustainability

The Croton lechleri tree is rapid growing and abundant in multiple countries in rainforest regions. We focus on the long-term sustainable management of the tree as part of our commitment to helping local communities conserve their natural resources while also earning income for the basic needs of their families such as food, clothing, health care and education. Our team members have practiced fair trade with our local and indigenous partners for more than two decades which has provided income-generating opportunities for individuals, communities and families. Across Peru, large numbers of Croton lechleri trees have been planted following harvesting in collaboration with communities and small local businesses.

HOW Canalevia-CA1 WORKS

Canalevia-CA1 treats CID by modulating the hypersecretion of CI ⁻ in diarrhea and normalizes fluid influx into the intestinal lumen. Secretory diarrhea (intestinal fluid secretion) is driven by active transepithelial CI ⁻ secretion, which creates the electrochemical force for paracellular Na+ secretion and the osmotic driving force for transcellular fluid secretion.

Dosage & Administration

60 tablets per bottle, 125mg of crofelemer per tablet. Administer one tablet orally twice daily for 3 days for dogs weighing up to 140 pounds. For dogs weighing more than 140 pounds, administer two tablets orally twice daily for 3 days. Tablets should be swallowed whole and should not be broken, crushed or chewed. If the dose is chewed, one additional dose may be administered.

IMPORTANT SAFETY INFORMATION

SAFFTY

For oral use in dogs only. Not for use in humans. Keep Canalevia®-CA1 (crofelemer delayed-release tablets) in a secure location out of reach of children and other animals. Consult a physician in case of accidental ingestion by humans. Do not use in dogs that have a known hypersensitivity to crofelemer. Prior to using Canalevia-CA1, rule out infectious etiologies of diarrhea. Canalevia-CA1 is a conditionally approved drug indicated for the treatment of chemotherapy-induced diarrhea in dogs. The most common adverse reactions included decreased appetite, decreased activity, dehydration, abdominal pain, and vomiting (Please click HERE for full prescribing information)
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.

Thoughts on the presentation

The information is very interesting and I like the sustainability and helping the local communities. I agree pet owners would love to know this information too.

This is a new approach to the marketing and would probably get clients asking for the drug.

Information would be valuable for pet-owners as they are drawn to natural sustainable resources.

Interesting information about sustainability practices; I get that question a lot when I discuss Stelfonta, and assume I would get the same question with Canalevia.

The background information on the drug is interesting and would really resonate with clients in a short pamphlet about the drug.

I agree with others that this information would be effective when marketing to clients.

It is good to see that the drug is considered to be a natural sustainable product which many of our clients are looking for.

Questions (concerns and clarifications)

Can we use this for more than 3 days, and if diarrhea not resolved, then is it likely the drug won't work?

As long as there is a prescription (or refill) for another 3 days of therapy, the answer is yes.

The reasonable expectation is that the drug would be effective within 1 full course of treatment (twice daily for 3 days). But we should also look for stool consistency improvements. A heavily diarrheagenic case could have some stool consistency improvement and that is an indication that the drug is somewhat effective even if the dog still presents with soft stools.

Can we start the drug prior to diarrhea starting?

Canalevia-CA1 is conditionally approved to treat chemotherapy-induced diarrhea (CID) in dogs and is not indicated for prophylaxis.

Is there any effort to have Canalevia approved for non-chemotherapy-induced diarrhea?

Not at the current time.

One question is whether or not all diarrhea caused is secretory. This is made for secretory diarrhea that we see in certain conditions but with chemotherapy, part of the diarrhea is due to destruction of the intestinal lining and I do not see that a drug for secretory diarrhea would be good for this as well.

We agree that this can be confusing. The active ingredient is not an "antisecretory agent". The molecule acts by inhibiting hypersecretion of CI- which can happen in any enterocyte. The mechanism by which CI- channels enter hypersecretion is multifactorial but for chemotherapy the focus is on the local inflammation caused by adjacent cell death.

Any experience of what was discussed.

We have in stock. Used it a few times. Results are unpredictable.

While my patients are on this drug, the diarrhea clears but often recurs off the drug as the causes of diarrhea in our cases are multifactorial and not always just chemotherapy induced. Any information on long term treatment? Can once a day dosing still work as well?

We cannot answer on the "once a day dosing" since this drug is currently under a Conditional Approval license. Canalevia-CA1 can ONLY be used as directed by the label.

As to the "long term" use, legally as long as there is a prescription (or refill) to keep treating dogs twice daily for 3 days, the animals could receive as many 3-day treatment cycles as needed. You will find in the package insert a couple of toxicology studies in dogs receiving long term exposure to the active ingredient with no serious adverse effects.

I agree with others. I have seen diarrhea improve on it, but then it worsens again when it's discontinued. It would be helpful to know if it can be administered for longer or at a tapering dose.

I have used it 5-10 times and have not found it to be more effective in helping with diarrhea. Many of the dogs will get diarrhea back once it is stopped and it can be expensive to continue to prescribe this drug. I agree that many of our patients often have more chronic diarrhea probably given that there is ongoing damage from treatment and also other factors such as diet changes and concurrent medications.

Thoughts for the future

(Disclosure - I am employed by QBiotics) - I recently had an oncologist tell me they were using Canalevia with Stelfonta as many patients get diarrhea with treatment. Not sure mechanism of diarrhea - MCT degranluation, systemic inflammation, concomitant medications related but, interesting to see if others are using and if it is effective?

Interested in long-term options for chronic diarrhea, Palladia-induced diarrhea especially!

I know this is specifically for chemotherapy induced diarrhea but data on a longer term regimen would be helpful.

I agree with the others. More data evaluating longer term use or use in other forms of secretory diarrhea would be helpful to support its adoption as a first-line diarrhea therapy.

I would like to see more clinical research on this drug to want to continue to use it in the future.

Good comments, points taken. As we have mentioned, there is long term data available in the package insert and repeat dosing is an option.





Not Juniper, but a few weeks ago we worked in an elephant sanctuary in Thailand. Bigger than a cat, but pretty cute none-the-less





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