

Message from the President



For the past several months, I have been spending a lot of time on the phone with dog owners asking about Immunocidin (Imm-you-know-sigh-din, our immunotherapy for treating canine mammary cancer.

Many of these folks have found out about the product through social media canine cancer support groups, the Canine Cancer Alliance (financial supporters of our Immunocidin research program) or word-of-mouth from others whose dogs have been treated with the product.

In most cases, these calls are lengthy because “pet parents” want to not only discuss their pet’s cancer diagnosis, but they want to tell me about their dog’s life and his/her importance to them. “Man’s best friend” is truly an apt description for these canine family members.

We’re lucky that we can offer a product that has proven safe and effective for the treatment of mammary cancer. Ongoing research suggests that other cancers may respond well to treatment with Immunocidin.

Dr. Jeannette Kelly, a veterinary oncologist in New Mexico, has the most experience with Immunocidin. She will often prescribe it as an adjunct therapy with chemo in dogs with various cancers. She will also prescribe it as a solo treatment in dogs with late-stage disease when lifesaving treatment is no longer an option. Her experience has shown that

the product is safe and offers improved quality of life in dogs with limited options.

Our research program with Immunocidin is very active. We have a number of veterinarians experimentally treating dogs with osteosarcoma (bone cancer) using our product. Other vets are using it to treat canine bladder cancer, squamous cell carcinoma, adenocarcinoma, B-cell lymphoma and soft tissue sarcoma.

I continue to be moved by the stories of the importance of canine family members in your lives and I welcome more of these. It’s heartwarming to know that pet parents will take extra steps and investment in improving the lives of their pets. We encourage you to ask your veterinarian about Immunocidin as a treatment option for your dog with cancer, or contact us directly for further information.

Amplimune Shown to Improve Fertility, Decrease Mastitis and Metritis

An article has been published in the Journal of Animal Science summarizing a research study conducted by Colorado State University researchers. They evaluated the effect of peripartur (around the time of calving) administration of mycobacterium cell wall fraction (MCWF) (Amplimune®) on the incidence of disease during early lactation and the subsequent fertility of organic-certified dairy cows.

In this study, cows were randomly assigned to either a treatment group (n=65) or control group (n=71). The treatment group received 5 mL of Amplimune by subcutaneous (SC) injection 7 days before expected calving, with a second dose within 24 hours after calving. The control group received a placebo (saline) at the same time points. Outcome variables that were analyzed included incidence risk of peripartur and early lactation health disorders, and pregnancy at first artificial in-



semination (AI), 100 days in milk (DIM) and 150 days in milk.

The CSU researchers found that the incidence rates of both clinical mastitis (bacterial infection of the udder) and metritis (uterine infection) before 28 DIM was lower in the Amplimune-treated group than in the control animals (clinical mastitis: 6.3% vs. 19.7%, respectively [a

68.6% reduction]; metritis: 36.9% vs. 50.7%, respectively [a 27.2% reduction]). Pregnancy was analyzed at three time points: first AI, 100 DIM and 150 DIM. In multiparous cows (animals having more than one pregnancy), the Amplimune-treated cows outperformed the control animals at all time points (35.6% pregnancy vs. 19.2% pregnancy at first AI; 51.1% vs. 25.0% at 100 DIM; and 64.4% vs. 40.4% at 150 DIM). Overall, median intervals from calving to pregnancy were 90 days in the Amplimune-treated group vs. 121 days in the control group.

These findings echo those of a Canada-based embryo transfer (ET) research group. Their study involved synchronized Holstein heifers receiving a single 5 mL dose of Amplimune by intramuscular (IM) injection on the day of heat, approximately one week prior to ET (control animals received no Amplimune).

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Amplimune Shown to Improve Fertility ... (cont'd)

Pregnancy per synchronized recipient at day 60 was greatly improved in the Amplimune group, with 131 of 292 heifers pregnant (45%) as compared to the control group, in which only 83 of 296 heifers were pregnant (28%). These data were presented at the 2021 International Embryo Technology Society (IETS) Virtual Conference (January 2021) and published in the journal, Reproduction, Fertility and Development.

The CSU research group noted that the incidence of respiratory disease in cows less than 28 DIM was greater in the Amplimune-treated group than in the control animals (0% vs. 7.7%). A number of these cases occurred in animals that were previously diagnosed with other diseases (puerperal metritis, clinical ketosis, acidosis, abomasal displacement) and the researchers speculated that these co-morbidities may have made the cows more susceptible to developing respiratory symptoms. The Company notes that this respiratory finding is unexpected, considering that MCWF products, including Amplimune, have been used for many years to treat and prevent respiratory diseases in domestic animals.

NovaVive has been working with a number of dairy producers to see if the CSU results can be replicated in other lactating cow herds. In data collected to date, the results are, in fact, being consistently repeated (see table below). Further assessment is ongoing, both following the CSU treatment regimen and other regimens.

Amplimune is approved by regulators in the USA, Canada, New Zealand and the

United Arab Emirates to reduce the clinical signs and mortality associated with *E. coli* K99 diarrhea in neonatal calves. The product is an emulsion of MCWF that enhances innate immunity to fight bacterial infections without the use of antibiotics. Amplimune is OMRI listed in the USA and Canada for use in organic production.

Amplimune Cumulative Average Results - 5 US Dairies and 1,355 cows		
	Absolute % Improvement	Relative % Improvement
Clinical Mastitis < 30 DIM	4.4%	44.6%
Clinical Metritis	7.6%	31.0%
Pregnancy 100 DIM	11.3%	28.9%
Pregnancy 150 DIM	6.8%	18.5%

Equine Respiratory Disease and Immunotherapy

According to the American Association of Equine Practitioners, equine influenza or other respiratory viruses (rhino-pneumonitis, rhino virus) or bacteria can strike a horse regardless of the time of year. Horses that are attending events or living in boarding barns where they are grouped with other horses are particularly at risk.

Like with humans, respiratory disease in the horse usually presents as a cough or discharge from the nose or eyes, often with listlessness. The first step is to check for fever, which would indicate a viral or bacterial infection in the lungs. If there's no fever, the symptoms could be caused by an allergic reaction to the environment or food.

If the horse has nasal discharge (sometimes called "the snots"), consider its appearance. A clear and watery discharge may be normal and not necessarily a problem, but it could signal a viral infection. An opaque, white discharge often indicates mucus and



may be related to an allergic reaction or airway inflammation. A nasal discharge with color (creamy, yellow, green) is usually indicative of bacterial infection.

Immunotherapy is designed to kick-start an animal's immune system to fight disease. NovaVive's line of regulator-approved immunotherapies includes Equimune[®], for the treatment of viral

equine respiratory disease complex (ERDC). Equimune is approved and available in the USA, Australia and New Zealand.

A single dose of Equimune, when administered by IV injection, stimulates the horse's innate and specific immune responses for several days.

Equimune activates immune system cells, thereby enhancing immediate production of interleukin 1 (IL-1). IL-1 then initiates both cell-mediated and humoral immunity cells. Cell-mediated immunity immediately seeks out virus-infected cells and destroys them. Humoral immunity results in antibody production to provide a longer lasting protection against the particular viral invader.

