Canine Parvovirus Monoclonal Antibody

Monoclonal antibody technology paves the way for a groundbreaking approach to this deadly virus

Jennifer Miller, DVM
Veterinary Technical Marketer, US Pet Health, Elanco Animal Health
After earning her DVM degree from Purdue, Dr. Jennifer Miller worked in small animal practices in the Chicago area and central Indiana before joining Elanco. After starting in Elanco's Product and Veterinary Support group, she currently works on the marketing team supporting Elanco's vaccine portfolio and Canine Parvovirus Monoclonal Antibody.

THE PROBLEM

Canine parvovirus (CPV) is a highly contagious disease that is transmitted by dog-to-dog contact and by contact with contaminated objects, surfaces and hands. The virus is heat-, cold-, humidity- and drying-resistant and can survive for long periods in the environment. CPV vaccines are highly effective and widely available, yet the disease is an ever-present threat for all dogs — especially puppies and unvaccinated dogs, which are at the highest risk.

The virus initially replicates in the oropharyngeal and mesenteric lymph nodes, and then enters cells by binding to a viral protein receptor on the cell surface. Inside the cell, the virus overtakes the cell's metabolism and quickly spreads to the rapidly dividing cells in the gastrointestinal (GI) tract, bone marrow and lymphoid tissues. CPV breaks down the blood–intestinal barrier, which causes GI bleeding, dehydration and hypovolemic shock, destroys young immune cells and allows bacteria to enter the bloodstream. Secondary infections and life-threatening sepsis can result. CPV can be deadly if left untreated.

Traditional CPV treatment involves intensive supportive care to combat dehydration and control vomiting and diarrhea. Some veterinarians treat CPV with hyperimmune plasma, but these products are not USDA-approved, are not proven to effectively treat CPV enteritis and require special administration supplies. Affected puppies and dogs must be kept in strict isolation to prevent disease transfer. Patients usually require 24/7 care and may require hospitalization for three to five days or longer. This high-cost treatment causes the pet owner significant emotional stress, with no guaranteed outcome for the pet.

THE SOLUTION

Scientists realized that CPV treatment needed a more direct

approach and turned their attention to targeted monoclonal antibodies, an emerging approach with about half the drugs being developed for human use based on this technology. Their goal was to design and produce monoclonal antibodies that bind to a specific viral protein, inhibiting the virus's ability to enter vulnerable cells, in hopes of improving CPV patient outcomes and providing faster illness resolution. Elanco's Canine Parvovirus Monoclonal Antibody (CPMA) was the end product.

THE INNOVATION

Elanco Animal Health research scientists developed CPMA in several steps. The antibody was encoded with DNA using a dog constant region and a rat variable region to create a chimeric antibody composed of antibody segments from two different species. The DNA encoding the parvovirus antibody was added to special cells to generate monoclonal antibodies, the monoclonal antibody was selectively removed from the cells and other proteins and material were washed away, leaving the CPMA. The rat variable domain is the most important CPMA component, since this is the region that directly interacts with the virus. CPMA binds to the CPV, inhibiting the virus from entering the host cell. CPV typically enters the host cell by binding to the host transferrin receptor, whereas CPMA binds on the same CPV location where the transferrin receptor typically interacts, blocking access. In addition, CPMA may work by destabilizing CPV, sequestering and aggregating virus particles and activating immune effector cells to phagocytize the virus.

Early studies demonstrated that CPMA prevented CPV from entering the host cell, effectively stopping the virus. CPMA was also studied in a CPV challenge setting that involved naïve 8-week-old dogs. In the study, the dogs were ill enough to demonstrate that the challenge model was effective, and dogs received either CPMA or a placebo. The CPMA-treated dogs experienced significantly faster times to resolution of vomiting, inappetence and lethargy. Also, no CPMA-treated dogs died from CPV.

CPMA offers CPV patients a targeted solution and can provide predictable outcomes. Treatment involves a single intravenous dose of 0.2 mL/kg that can shorten the disease course, improve patient outcomes and allow dogs to return home sooner. The treatment may also be beneficial for veterinary teams, who can face increased workload and emotional distress caused by CPV treatment failure.

A field safety study involving 147 client-owned dogs from 6 weeks to 15 years of age showed that CPMA is well tolerated in healthy dogs. No dogs exhibited anaphylactic reactions or clinical signs consistent with anaphylaxis.

Elanco was granted conditional USDA approval for CPMA, because no treatment that addresses CPV was available, and the disease poses a serious threat to dogs, resulting in significant morbidity and mortality. The conditional approval status means that CPMA is properly manufactured, is well tolerated and can reasonably be expected to be effective when used according to the label instructions. Elanco completed safety and efficacy studies as they developed the product for approval. A validated potency test is the missing piece for full licensure. Elanco has performed internal potency assay validation, and the USDA is reviewing those test methods for validation. Potency testing indicates the product is consistently in the vials at the concentration per the outline of production. Once the USDA has validated the proposed testing methodology, the product will be eligible for full approval. CPMA is the first and only USDA conditionally approved medication that targets parvovirus directly. One intravenous dose can shorten the disease course, improve patient outcomes and may reduce emotional stress.

THE DIFFERENCE MAKER

Elanco's Canine Parvovirus Monoclonal Antibody is the first therapeutic solution to receive conditional USDA approval for the treatment of canine parvovirus.