Clinical testing for Viroplazin broad spectrum antiviral medication

Study Title:

A Multi-center, Randomized, Double-blind, Placebo-controlled Clinical Test Evaluating the Efficacy and Safety of Viroplazin in Dogs and Cats with Multiple Viral Diseases (Parvovirus Gastroenteritis, Distemper in Dogs; Rhinotracheitis, Calicivirus, Panleukopenia in Cats).

Objective:

Evaluate the efficacy and safety of Viroplazin in different species with different viral diseases compared to placebo . Keeping ethical standard care in the treatment of specific viral infections in Viroplazin treated and placebo treated groups .

Study Design:

- Multi-center, randomized, double-blind, placebo-controlled trial.
- Parallel-group design with two arms: Viroplazin vs. Placebo.

Study Population:

- Dogs diagnosed with Parvovirus Gastroenteritis or Distemper
- Cats diagnosed with Rhinotracheitis, Calicivirus, or Panleukopenia.
- Age: older than 3 weeks
- Both sexes, all breeds.

Inclusion Criteria:

- Confirmed diagnosis via PCR or antigen test for respective viruses.
- Clinical signs consistent with disease diagnosis.
- Owner consent obtained.

Exclusion Criteria:

- Severe comorbidities (e.g., severe renal or hepatic dysfunction, uncontrolled bacterial or parasitic infection).
- Prior antiviral or immune-modulating treatment within 7 days before enrollment.
- Pregnant or lactating animals.
- Known hypersensitivity to Viroplazin ingredients.

Randomization and Blinding:

- Randomization 1:1 to Viroplazin or placebo groups with current standard of care , symptomatic treatment in both group equally. /like; IV fluid for dehydration , Antiemetics for vomiting , Oxygen support if respiratory symptoms are sever, pain and fever management /
- Blinding maintained for owners, veterinarians, and trial staff.

Treatment Administration:

- Viroplazin/Viroplazin placebo.
- dose: According to body weight; 5 mg per kg body weight, administered orally 3 times daily for 7 consecutive days.
- Placebo: Visually matched inert substance administered identically.

Outcome Measures:

Primary Efficacy Endpoints:

- Resolution of clinical signs from Day 1 to Day 7, assessed daily using clinical scoring systems specific for each viral disease.
- Virus clearance rate measured via PCR/Antigen testing at Days 4 and 7.

Electronic Case Report Forms (eCRFs) for Standardized Data Collection:

First step is the determination of the clinical severity of the viral infection based on the clinical symptoms /1-5/ 5 being the most sever at the beginning of the start of treatment . Second step is to determine how long the current symptoms has been going on . /how many hours or days of each pet has been sick with the diagnosed disease / This is essential for the interpretation of the result of the treatment . Randomization must include the same severity level at starting of treatment for both Viroplazin and Placebo.

Dog Electronic Case Report Forms (eCRFs):

- **Parvovirus Gastroenteritis eCRF:** Clinical signs (Fever , vomiting frequency, diarrhea frequency, blood in feces, appetite, hydration, activity level).
- **Distemper (eCRF):** Clinical signs (Fever , respiratory signs frequency, neurological signs presence, gastrointestinal signs, ocular discharge, activity level).

Cat eCRFs:

- **Rhinotracheitis eCRF:** Clinical signs (sneezing frequency, ocular discharge, nasal discharge severity, fever, appetite, hydration, activity level).
- **Calicivirus eCRF:** Clinical signs (oral ulcer presence and severity, drooling, respiratory signs, fever, appetite, activity level).
- **Panleukopenia eCRF:** Clinical signs (Fever , vomiting frequency, diarrhea frequency, blood in feces, leukopenia severity, hydration, activity level).

Each eCRF will include standardized scoring:

Scoring Scale (0-6):

- **0** = Absent (no signs)
- **1** = Mild (occasional/intermittent signs)

- **2** = Moderate (frequent signs, but responsive to supportive care)
- **3** = Severe (persistent, unresponsive signs)
- 4 = Very Severe
- 5 = Critical /near death/
- 6 = Dead

Secondary Efficacy Endpoints:

- Time to clinical improvement (reduction of primary clinical signs by ≥50%).
- Number of days the animal become symptom free
- Mortality rate at Day 14.
- Recurrence or worsening of symptoms within 14 days.

Safety Endpoints:

- Frequency and severity of adverse events (AEs).
- Precise description of the adverse event (AE) .
- Changes in hematological and biochemical parameters from baseline to Day 7 and Day 14.
- Withdrawal rate due to adverse events (number of animals forced to quit treatment because of unexpected adverse events).

Sample Size:

- Total of 100 dogs and 100 cats for each of the viral diseases (50 per treatment group and 50 for placebo with standard care), ensuring statistical power of ≥80%.

Statistical Analysis: / this will be done by dr Sichnik/

- Intent-to-treat and per-protocol analyses.

- Primary endpoint comparison via Chi-square or Fisher's exact test.
- Kaplan-Meier method for time-to-event analyses.
- Safety analyzed descriptively.

Data Management:

- Electronic Case Report Form (eCRF) for standardized data collection.
- Regular monitoring visits to ensure protocol adherence and data accuracy.
- Digital photograph demonstration of each patient with name tag and clinical symptoms and medical record, and laboratory reports .

Ethical Considerations:

  - Study conducted in compliance with EMA and FDA guidelines, Good Clinical Practice (GCP), and the Declaration of Helsinki principles adapted for veterinary use.

- These are ;
- Obtained a Ethics committee approval from Pakistani Veterinary school before trial initiation.
- The principal investigator received a Good Clinical Practice (GCP) certificate. /online ,free , about 4-6 hours study and a test at the end /
- Owner consent form sighed by owner.
- Clinical protocol ensuring standard-of-care. / fluid, antibiotic /
- Follow the the withdrawal criteria and follow-up care guidelines .

Study Duration:

- Recruitment period:3- 12 months. depending on case load.
- Treatment and follow-up period: 14 days per enrolled animal.

- Total study duration: Approximately 6-8 months including data analysis and reporting.

Reporting:

Each participating animal need to have a name tag for identification,

- Every pet need to be photographed/filmed that is participating in the study with the eCRF showing the name and initial scoring of clinical symptoms for both Viroplazin treated and placebo group.
- Every pet need to be photographed/filmed that is participating in the study with the eCRF showing the name and final scoring of clinical symptoms at the end of treatment or if died the deceased animal .
- Send for interim analysis after 50% enrollment with picture