**Supplementary Material**

**Table S1.** Inclusion, exclusion, and elimination criteria.

| Inclusion criteria | • Any breed and sex under six months of age  
|• The appearance of clinical signs within a period no longer than 48 hours before consultation or diagnosis  
|• Minimum weight of 1 Kg  
|• Two or more clinical criteria for systemic inflammatory response syndrome (hypothermia < 37.8 °C or fever > 39.4 °C, tachycardia >140 bpm, tachypnea >30 rpm, and leukopenia < 5.5 x 10⁹/L or leukocytosis > 12.5 x 10⁹/L)  
|• Necessary hospitalization  
|• Owners willing to participate in the clinical trial with a signed informed consent letter |
| Exclusion criteria | • Hospitalization under the observation of another veterinarian outside recruiting veterinary clinics/hospitals  
|• Necessary application of another immunomodulator or granulocytic colony-stimulating factor based on clinical evidence and at the discretion of a veterinarian |
| Elimination criteria | • Any adverse effects to administration of immunomodulator  
|• Suspended administration of immunomodulator  
|• Death within 24 hours after hospitalization |
Table S2. Conventional treatment of the study population. Treatments were classified according to their action mechanism. The number of puppies that received each of the treatments is specified.

| Treatment classification | Conventional treatment + vehicle n= 10 | Conventional treatment + immunomodulator n= 16 |
|--------------------------|----------------------------------------|-----------------------------------------------|
| Fluid therapy            | 0.9% NaCl solution 10/10               | 0.9% NaCl solution 16/16                      |
| Antibiotics              |                                        |                                               |
| Ampicilin                | 4/10                                   | Ampicilin 2/16                                |
| Metronidazole            | 4/10                                   | Metronidazole 10/16                           |
| Enrofloxacin             | 2/10                                   | Enrofloxacin 2/16                             |
| Cephalexin               | 4/10                                   | Clindamycin 2/16                              |
| Sulfa-trimethoprim       | 3/10                                   | Sulfa-trimethoprim 4/16                       |
| Antiemetics              |                                        |                                               |
| Maropitant citrate       | 7/10                                   | Maropitant citrate 11/16                      |
| Metoclopramide           | 4/10                                   | Metoclopramide 5/16                           |
| Ondansetron              | 2/10                                   |                                               |
| Antiespasmodics          | Prinifial 3/10                         | Butylhioscine 6/16                            |
| Gastric mucosa protectors| Ranitidine 5/10                        | Ranitidine 8/16                               |
|                          | Omeprazole 7/10                        | Omeprazole 14/16                              |
|                          |                                        | Sucralfate 5/16                               |
| Analgesics               | Buprenorphine 7/10                     | Buprenorphine 10/16                           |
|                          | Meloxicam 2/10                         | Meloxicam (infusion) 3/16                     |
|                          | Lidocaine (infusion) 1/10              | Metamizole 3/16                               |
| Parenteral nutrition     | 0.5% Dextrose and aminolyte 8/10       | 0.5% Dextrose and aminolyte 10/16             |
Table S3. Demographic characteristics of the study population.

| Group                                      | Age | Sex  | Breed     | # of puppies |
|--------------------------------------------|-----|------|-----------|--------------|
| Conventional treatment + vehicle           |     |      |           |              |
| Months # of puppies                        |     |      |           |              |
| 2   3                                      | Female | 1 | Mixed     | 3            |
| 3   3                                      |       |   |           |              |
| 4   2                                      | Male  | 9 | Pure breed | 7            |
| 5   1                                      |       |   |           |              |
| 6   1                                      |       |   |           |              |
| Conventional treatment + immunomodulator    |     |      |           |              |
| Months # of puppies                        |     |      |           |              |
| 2   3                                      | Female | 8 | Mixed     | 7            |
| 3   2                                      |       |   |           |              |
| 4   5                                      | Male  | 8 | Pure breed | 9            |
| 5   3                                      |       |   |           |              |
| 6   3                                      |       |   |           |              |