

EFFICACY OF AIVLOSIN® WATER SOLUBLE GRANULES FOR THE **CONTROL OF ILEITIS IN SWINE**

SUMMARY

- ▶ An extensive clinical study evaluated the efficacy of AIVLOSIN® Water Soluble Granules for the control of ileitis in pigs challenged with virulent *Lawsonia intracellularis*.
- ▶ Compared to non-medicated controls, AIVLOSIN® significantly ($P < 0.001$) reduced the severity of clinical signs of PPE.
- ▶ 14.9% of control pigs died, but no PPE mortality occurred in AIVLOSIN®-treated pigs.
- ▶ AIVLOSIN® significantly ($P = 0.0103$) reduced the severity of gross intestinal PPE lesions, and significantly ($P < 0.02$) decreased the frequency of positive PCR and IHC samples.
- ▶ ADG improved 54.8% ($P = 0.0051$) and feed/gain improved 24.2% ($P < 0.0001$) in pigs medicated with AIVLOSIN®.
- ▶ AIVLOSIN® Water Soluble Granules is highly effective for the treatment of ileitis.

Porcine proliferative enteropathy (PPE, or ileitis) is an important enteric disease of pigs caused by the obligate intracellular bacterium *Lawsonia intracellularis*.¹ PPE remains endemic on the majority of swine farms despite various interventions. The chronic form of PPE typically occurs in growing pigs at 6 to 20 weeks of age, causing reduced rates of weight gain and increased variability in body size.

The economic impact of this endemic production disease can be very significant due to a longer fattening period, resulting in extra feed and building space required by affected pigs, in addition to death losses of high-investment older pigs.

Antimicrobial treatment remains the primary recourse for control of clinical ileitis outbreaks. AIVLOSIN® Water Soluble Granules, from Pharmgate Animal Health, is a water-soluble formulation containing tylvalosin, a macrolide antibiotic with potent activity against *L. intracellularis*.

AIVLOSIN® is indicated for control of PPE in groups of swine in buildings experiencing an outbreak of this disease, when administered at 50 ppm in drinking water of swine for 5 consecutive days. Tylvalosin has a unique chemical structure that enables the drug to penetrate intestinal epithelial cells more efficiently than other macrolide agents such as tylosin or tilmicosin.² In addition, tylvalosin has been demonstrated to sequester in neutrophils, enhance metabolic activation of macrophages, and offer beneficial anti-inflammatory and immunomodulatory effects.^{2,3} Together, these characteristics distinguish AIVLOSIN® as the new standard for ileitis control.

An extensive clinical study was conducted to evaluate the efficacy of AIVLOSIN® Water Soluble Granules for the control of ileitis in pigs experimentally infected with *L. intracellularis*.^{4,5}

EXPERIMENT DESIGN

The multicentric challenge study was conducted at 3 independent sites in North America (2 in U.S., 1 in Canada), with each site following a common study protocol. The study involved 288 weaned commercial hybrid barrows and gilts approximately 5 weeks of age (18-46 lb) acquired from high-health-status farms.

At each site, 96 pigs were assigned to 8 gender blocks based on body weight (randomized complete block design, 12 pigs of same gender and similar weight in each block). Within each block pigs were randomly allocated to 2 pens (6 pigs per pen) that were randomly assigned to either of 2 treatment groups:

- Non-medicated control (no medication);
- AIVLOSIN® (50 ppm tyvalosin administered in drinking water for 5 consecutive days).

Following acclimation, all pigs were orally challenged with an intestinal mucosal homogenate prepared from a recent field case of acute hemorrhagic PPE using a well characterized and validated challenge model.⁶ Each pig was dosed via intragastric gavage with approximately 1.8×10^8 to 1.3×10^9 *L. intracellularis* organisms.

AIVLOSIN® treatment via the drinking water was initiated when at least 15% of pigs were observed to be clinically affected with PPE (4-6 days post challenge).

Data collected during a 22-day post-treatment phase included assessment of PPE clinical parameters, mortality, gross intestinal lesions, average daily gain (ADG), feed efficiency (feed/gain), polymerase chain reaction (PCR), and immunohistochemistry (IHC).

All surviving animals were euthanized on day 22, fecal samples collected at necropsy for PCR analysis, ileal samples collected for IHC analyses, and intestinal tracts scored for gross PPE lesions. Suspected PPE mortalities were confirmed based on lesion scoring.

All data from the 3 sites were pooled and analyzed using appropriate statistical methods.

RESULTS

AIVLOSIN® significantly reduced the percent of abnormal pig-days for all 3 clinical PPE parameters [abdominal appearance ($P = 0.0005$), demeanor ($P = 0.0002$), fecal consistency ($P = 0.0001$)] compared to the non-medicated control group (Figure 1). Notably, the incidence and duration of abnormal fecal consistency scores was reduced 40.2% by AIVLOSIN® treatment.

Mortality was significantly reduced ($P < 0.0001$) from 14.9% in the control group to 0% in AIVLOSIN®-medicated group (Figure 2). The mean gross lesion score of the AIVLOSIN®-treated pigs (0.24) was significantly lower ($P = 0.0103$) than that of the control group (0.69), further documenting the ability of AIVLOSIN® to protect pigs from pathology induced by ileitis.

Compared to controls, AIVLOSIN® significantly ($P < 0.02$) decreased the frequency of PCR and IHC samples positive for *L. intracellularis* (Figure 3). The decreased frequency of positive fecal PCR samples collected at the end of study indicates that fecal shedding of *L. intracellularis* was reduced in AIVLOSIN®-medicated pigs compared to untreated animals. Reduced fecal excretion will lessen environmental contamination with disease organisms. This gives less opportunity for disease transmission to exposed penmates.

The reduction of positive IHC samples in AIVLOSIN®-medicated pigs further suggests that treatment helped limit intestinal damage, complementing the reduced severity of gross intestinal lesions shown in Figure 2.

As a result of the excellent ileitis control provided by AIVLOSIN®, performance parameters were favorably impacted in treated pigs compared to controls (Figure 4). Pigs medicated with AIVLOSIN® generated a significant 54.8% ($P = 0.0051$) improvement in ADG during the 22-day post-treatment period and feed/gain was significantly improved 24.2% ($P < 0.0001$) in treated pigs compared to non-medicated controls.

These outcomes illustrate the adverse economic impacts ileitis can impose on swine productivity (in addition to costly death losses), and confirm the ability of AIVLOSIN® to help support performance during a severe outbreak of clinical disease.

IMPLICATIONS

Study results verify that AIVLOSIN® administration at 50 ppm in drinking water for 5 consecutive days is highly effective for the control of PPE. AIVLOSIN® significantly improved all ileitis assessment parameters in susceptible young pigs that received a severe *L. intracellularis* challenge infection.

Performance parameters (ADG, feed/gain) were also significantly improved as a result of the excellent PPE control provided by AIVLOSIN®.

Previous research has documented the ability of tyvalosin to quickly achieve high intracellular concentrations in epithelial cells and neutrophils.²

Continued

This favorable pharmacodynamic behavior is particularly beneficial for treating intracellular pathogens like *L. intracellularis* and probably contributed to the superb clinical efficacy demonstrated in this study.

The reduced fecal shedding of *L. intracellularis* by AIVLOSIN®-treated pigs in this study suggests that the antibiotic may contribute to a reduction in environmental contamination. This is an important factor in the control of PPE in affected herds since disease risk and severity often correlates with the intensity of pathogen challenge pigs encountered in the production unit.

CONCLUSIONS

This clinical challenge study demonstrated that AIVLOSIN® administration in drinking water is effective in reducing clinical signs, mortality, intestinal lesions, *L. intracellularis* fecal shedding, and performance suppression associated with PPE.

Furthermore, the clinical efficacy, reduced fecal shedding, low therapeutic dose rate, and brief treatment duration are all in accordance with best practices for contemporary commercial swine units. ■

Important Safety Information: Available under prescription only. AIVLOSIN is indicated for the control of swine respiratory disease (SRD) associated with *Bordetella bronchiseptica*, *Haemophilus parasuis*, *Pasteurella multocida* and *Streptococcus suis*, or porcine proliferative enteropathy (PPE) associated with *Lawsonia intracellularis*, in groups of swine in buildings experiencing an outbreak of either disease. For use only in drinking water of pigs. Not for use in lactating or pregnant females, or males and females intended for breeding. People with known hypersensitivity to tylosin tartrate should avoid contact with this product. When used in accordance with label directions, no withdrawal period is required before slaughter for human consumption.

References

- 1 McOrist S et al. Int J Syst Bacteriol 1995; 45:820-825.
- 2 Stuart AD et al. Pig J 2007; 60:26-35.
- 3 Moges R et al. Exp Biology 2017; 31: 469-7.
- 4 ECO Animal Health study US.EFF 070142, data on file.
- 5 ECO Animal Health study US.EFF 090-170, data on file.
- 6 Winkelman NL et al. J Swine Health Prod 2002; 10:106-110.

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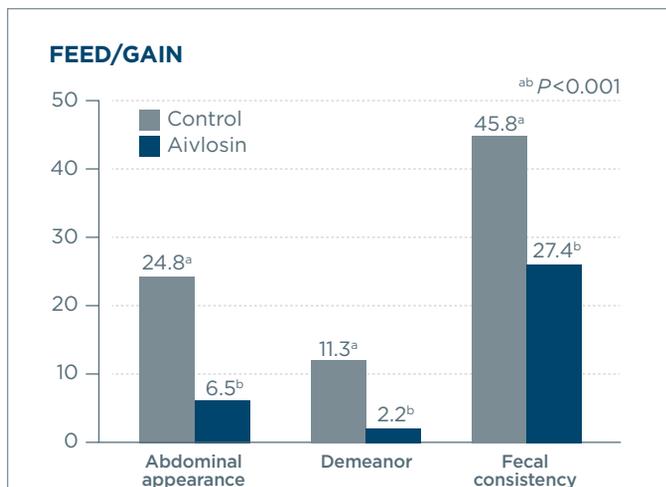


Figure 1. Mean percent of abnormal pig days (clinical scores)

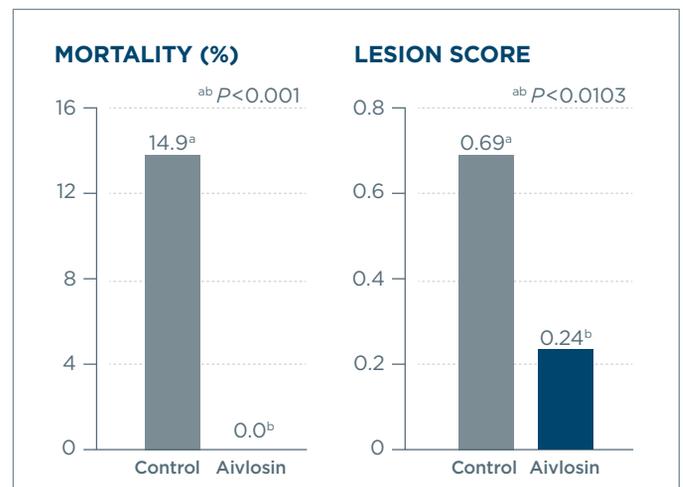


Figure 2. Mean PPE mortality and gross intestinal lesion scores (scored on a range of 0=normal to 3=severe)

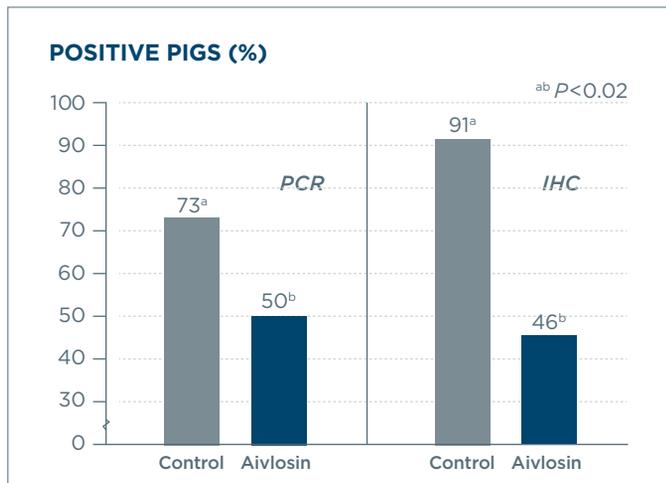


Figure 3. Percent of pigs at study conclusion testing positive for *L. intracellularis* by fecal PCR and ileal IHC

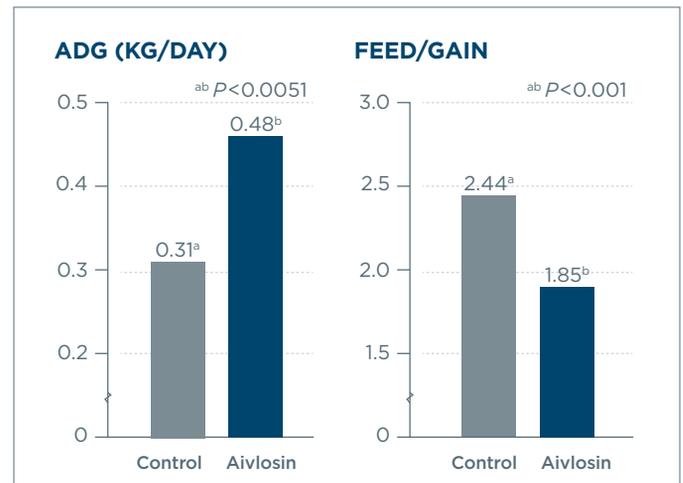


Figure 4. Mean pen average daily gain and feed efficiency