Efficacy of a novel inactivated Lawsonia intracellularis vaccine

Lawsonia intracellularis causes Porcine Proliferative Enteropathy (PPE), also known as porcine ileitis. It is an infectious enteric disease characterised by thickening of the intestinal mucosa. Symptoms include diarrhoea, variation in batch sizes, a reduction in average daily weight gain (ADWG), increased feed conversion ratio and mortality.

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Sub-clinical infection may occur without the clinical signs of infection, but still result in reduced growth performance. Lawsonia intracellularis causes major economic loss to the swine industry. In the UK, ileitis causes losses between £2 million and £4 million per year.

In the EU, a live attenuated vaccine against Lawsonia intracellularis is commercially available, however, this is not compatible with antibiotics and has no claims for associated use with PCV2 and M Hyo vaccines.

In response, Porcilis Lawsonia was developed, the inactivated vaccine is compatible with Porcilis PCV M Hyo. The vaccine consists of a freeze-dried Lawsonia antigen and the solvent containing the adjuvant (Emunade).

The Lawsonia antigen can be reconstituted either with the Emunade adjuvant for stand alone use or can be reconstituted with Porcilis PCV M Hyo, for use as a combination vaccine. As both these vaccines need administering at the same target age, the preferred solution is to vaccinate against all three pathogens at the same time, ideally via one single injection.

Study objectives

- Assess the stand alone efficacy of Porcilis Lawsonia vaccine in comparison to the commercially available, live-attenuated vaccine against Lawsonia intracellularis challenge.

Additionally, the mixed-use of Porcilis Lawsonia with Porcilis PCV M Hyo was tested in the challenge model.

- To test Porcilis Lawsonia in a field trial on-farm with Lawsonia intracellularis associated mortality.

Materials and method

1. Experimental vaccine challenge trial

Three studies were performed, each with a similar design (Table 1).

Pigs were from a farm known to be negative for M Hyo and PRRSV and no history of Lawsonia intracellularis infection. 75 piglets per study were randomly allocated into three groups, each with 25 piglets.

- **Group 1:** Vaccinated i/m with 2ml Porcilis Lawsonia at four weeks of age (studies 1 and 2), or, with 2ml Porcilis Lawsonia in combined use with Porcilis PCV M Hyo at five weeks of age (study 3).

- **Group 2:** Vaccinated orally with 2ml live attenuated vaccine at four weeks of age (studies 1 and 2), or at five weeks of age – this group also received 2ml of PCV2 M Hyo vaccine combo i/m at three weeks (study 3).

- **Group 3:** Unvaccinated controls.

The challenge strain of Lawsonia intracellularis was obtained from homogenised infected intestinal mucosa and administered orally at four weeks post vaccination (study 1), 17 weeks post vaccination (study 2) or three weeks after last vaccination (study 3). The pigs were weighed weekly and observed daily for clinical signs of ileitis throughout the post challenge period. All pigs were euthanised 21 days post challenge.

Serum samples were collected at vaccination, challenge and necropsy. Additionally, faecal samples were collected at necropsy and tested for Lawsonia specific qPCR. The intestines, and ileum, were checked macroscopically for Lawsonia intracellularis infection and ileum samples were tested by qPCR and immuno-histological scores (IHC).

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Group	Study 1 & 2 Vaccinated at 4 weeks	Study 3 Vaccinated at 5 weeks	Age at challenge (weeks)
1	PL + Emunade 2ml	PL + Porcilis PCV M Hyo 2ml	8
2	Oral Vacc. 2ml	Oral Vacc. x 5w; PCV2 M Hyo combo x 3w	21
3	Unvaccinated control	Unvaccinated control	8

Table 1. Design of experimental vaccine challenge trial. Porcilis Lawsonia can be reconstituted either with Emunade or Porcillis PCV M Hyo.

Table 2. Post challenge results ± SD of vaccination challenge trials 1, 2 and 3.

Vaccine group		Avg clinical score/day 13-20	ADWG g/day 13-20	PCR faeces avg log pg DNA/µl/day 21	PCR mucosa avg log pg DNA/µl/day 21
Study 1	PL + Emunade	0.3 1.2[e]	935 ± 306[e,f]	0.23 ± 0.64	0.18 ± 0.43[f]
	Oral vaccine	0.9 ± 2.3[e]	655 ± 385	0.60 ± 0.82	0.66 ± 0.84
	Control	4.4 ± 6.5	550 ± 460	0.34 ± 0.62	0.57 ± 0.56
Study 2	PL + Emunade	3.0 ± 5.5	649 ± 751[e,f]	0.27 ± 0.54	0.71 ± 0.76[e]
	Oral vaccine	2.8 ± 5.8	-229 ± 1301	0.11 ± 0.38	1.05 ± 0.84
	Control	5.7 ± 5.5	-655 ± 723	0.46 ± 0.70	1.36 ± 0.57
Study 3	PL + PCV M Hyo[2]	1.5 ± 2.6	1012 ± 302[e,f]	1.37 ± 1.17[e,f]	1.10 ± 0.42
	Oral vaccine[b]	3.9 ± 4.4[e]	549 ± 597	2.43 ± 0.98	1.10 ± 0.51
	Control	1.0 ± 2.9	537 ± 627	2.47 ± 0.78	1.06 ± 0.49

[a] Porcilis PCV M Hyo. [b] Commercially available PCV M Hyo vaccine also applied. [c] Diarrhoea scoring. [e] $p < 0.05$ vs control. [f] $p > 0.05$ vs live vaccine.

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2. Field trial

This field trial was conducted in a commercial pig herd in the Netherlands with a known history of ileitis associated mortality, i.e. acute ileitis occurring from 20 weeks of age. A total number of 2,867 pigs were included, 50% (1,435) were vaccinated with Porcilis Lawsonia and then co-habited with the unvaccinated pigs.

The study continued for eight months, during which time all new batches of pigs were included in the study until slaughter at approximately 26 weeks of age.

Key performance parameters, i.e. overall mortality, ADWG and feed conversion rate were determined for the whole herd for historic comparison.

Results

1. Experimental vaccine challenge trial

In all three studies, the control animals developed signs of ileitis infection in the third week post-challenge; characterised by diarrhoea, reduced weight gain and bacterial shedding in faeces.

The infection was confirmed by necropsy (mucosal reddening and thickening), positive PCR and immunohistological ileum lesion scores. In comparison, pigs vaccinated with Porcilis Lawsonia showed a statistically significant reduction in clinical signs, weight loss and macroscopic and microscopic ileum lesion scores when compared to controls.

2. Field trial

After the start of the study, the Lawsonia intracellularis associated mortality was reduced to zero in the vaccine group, whereas 11 animals died or were culled due to acute ileitis in the control group ($p<0.0001$).

Furthermore, the total mortality during the study was significantly reduced in the vaccinates compared to the controls ($p=0.0335$).

For practical reasons the overall mortality (study pigs and non-study pigs), average daily weight gain and feed conversion rate were determined for the whole herd (derived from the farm data management system) and therefore could only be compared historically. The overall mortality decreased from 3.8% (year preceding the study) to 2.3% during the study period.

The ADWG gradually increased from 833g/day (year preceding the study) to 890g/day at the end of the study.

The feed conversion rate (kg feed/kg body weight) gradually decreased from 2.47 (year preceding the study) to 2.21 in the last two months of the study.

Discussion

The results of the studies demonstrate that an inactivated vaccine administered intramuscularly is highly efficacious against Lawsonia infection. This is in line with the previous results of Roerink et al. 2018 who demonstrated good protection against experimental Lawsonia intracellularis infection using inactivated whole cell vaccine.

The inactivated vaccine gave superior protection when compared to a commercially available live vaccine.

The results obtained in studies 1 and 2 demonstrate a similar level of protection to those in study 3, indicating that the PCV and M Hyo antigens do not have a negative effect on the efficacy of the Porcilis Lawsonia.

It should be noted that the improvements obtained in the field trial are an underestimation of the real effect as they were calculated for the whole herd, whereas only half of the pigs were vaccinated. If the whole herd were vaccinated, the improvement of the key production parameters would likely have been better, not only by the direct effect of vaccination but also by additional indirect effects as described by Knight Jones et al. 2014.

These indirect effects may result from reduced shedding, as shown in the experimental studies, and subsequent reduced infectious pressure.

Conclusions

In this study we show that the inactivated vaccine Porcilis Lawsonia, either as stand alone, or in mixed use with Porcilis PCV M Hyo, induced statistically significant protection against experimental Lawsonia intracellularis infection.

This was demonstrated by lower clinical scores, improved weight gain, reduction of Lawsonia intracellularis shedding and reduction of macroscopic and microscopic ileum lesion scores, when compared to control animals.

In the field trial, the vaccine proved to be highly efficacious; reducing Lawsonia intracellularis associated mortality to zero and improving key production parameters. ■

References are available from the author on request