The effect of water medication for PRRS-positive pig herds

Porcine Reproductive and Respiratory Syndrome (PRRS) is recognised as the most endemic and economically important disease of swine worldwide. Any effort directed towards the control of PRRS will have an important impact on the health status of pig herds and on the profitability of the swine industry.

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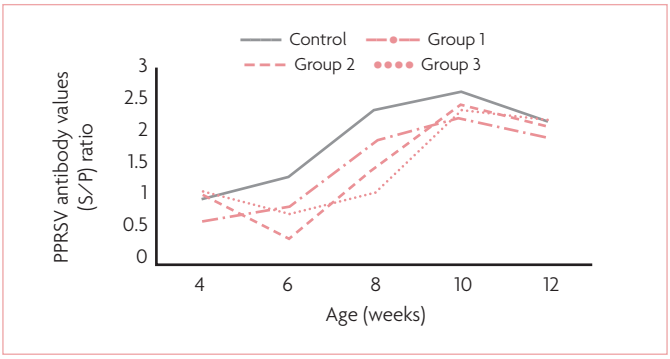


Fig. 1. PRRSV ELISA S/P ratio of the four treatment groups (Taiwan study).

It has been demonstrated that tilmicosin exhibits PRRSV-antiviral activities when concentrated in the pulmonary alveolar macrophages.

The rapid uptake of tilmicosin throughout the respiratory tract of pigs and the highest intracellular accumulation in lung macrophages versus other macrolide antibiotics is the basis for Tilmovet's tilmicosin PRRSV replication blocking effect and its high antibacterial activity.

In several trials using PRRSV infected pigs, a reduction of PRRS clinical signs and performance improvements were shown in tilmicosin-medicated pigs.

The majority of these studies are based on experimental PRRSV infections with animals medicated with tilmicosin via feed. Studies during which tilmicosin was administered via medicated water to control PRRS infection after PRRSV inoculation or in naturally infected weaned pigs are limited. The objective of this article is to describe the results of two Tilmovet water medication studies conducted post-weaning in PRRS infected herds with PRRSV viraemic pigs.

PRRSV pathogen and vaccination

Besides PRRSV-Type 1 (European subtype) and PRRSV-Type 2 (American subtype) various types and varieties of PRRSV can be found, which is due to ongoing mutation and recombination processes of PRRSV. As a consequence, highly pathogenic variants are created which, for example, can be found in Spain (Rosalia) or in China.

It is well known that Pulmonary Alveolar Macrophages (PAMs) are the primary target of PRRSV infection and the location of virus replication.

PRRSV vaccines currently available have many limitations in terms of heterologous protection. Vaccines cannot eliminate the PRRS virus. In the case of highly aggressive virus types (Rosalia Type), insufficient immune response of vaccines leads to failure in PRRS protection, creating more complex infections often associated with PRDC.

Tilmovet activities and antiviral effect

Tilmicosin is the active substance in Tilmovet and is characterised by a broad range of activities:

- Intracellular accumulation (macrophages, neutrophils, epithelial cells, enterocytes, leucocytes) and activity.
- Antimicrobial activity (Actinobacillus pleuropneumoniae, Mycoplasma hyopneumoniae, Glaeserella parasuis, Pasteurella multocida, Bordetella bronchiseptica).
- Antiviral activity (PRRS).
- Anti-inflammatory effect.
- Immunomodulatory properties.

Tilmovet provides unique pharmacokinetic activities when orally administered in pigs. Low serum concentrations, medium lung concentrations but very high alveolar macrophage concentrations lead to high presence at the respiratory infection sites. Tilmovet (tilmicosin) accumulates rapidly in the lysosome of macrophages and neutrophils due to ion trapping.

The intracellular accumulation of tilmicosin (75:1) is much higher in comparison to other macrolide antibiotics like tulathromycin (28:1), tylosin (21:1), tylvalosin (12:1) or erythromycin (6:1). The two to six times higher intracellular accumulation of tilmicosin is the key factor for its high antimicrobial and antiviral effect.

Tilmicosin studies have shown that the PRRSV replication inhibition effect in alveolar macrophages is dose dependent and that the clinical and pathological effect of PRRSV infection is significantly reduced after both feed medication and water medication. In the majority of these studies, animals were experimentally infected with PRRSV and medicated with tilmicosin via

Fig. 2. Survival rate age week 4 to 10 (Taiwan study).

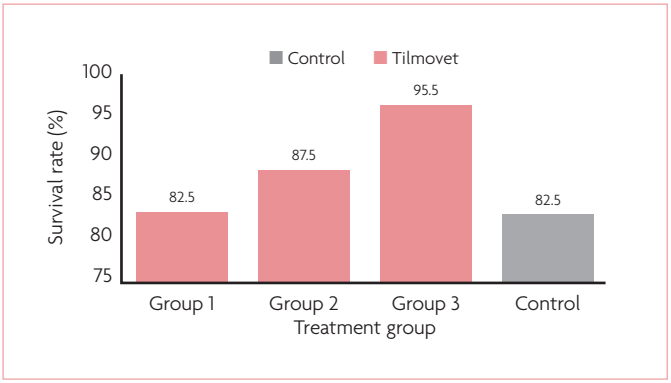


Fig. 3. Evaluation of the viral load of PRRSV-negative piglets at study start, from the beginning to the end of the experimental trial (Spain study).

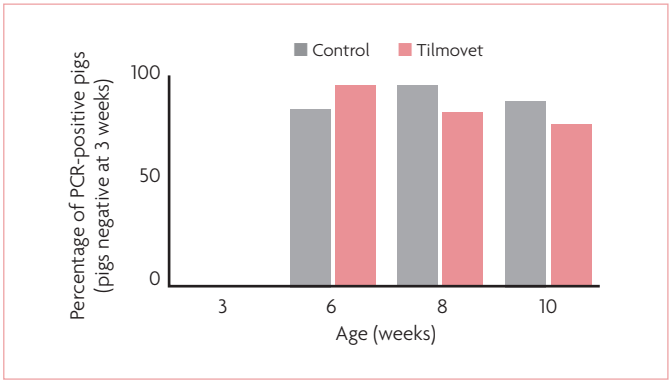


Fig. 4. Evaluation of the viral load of low positive piglets at study start, from the beginning to the end of the experimental trial (Spain study).

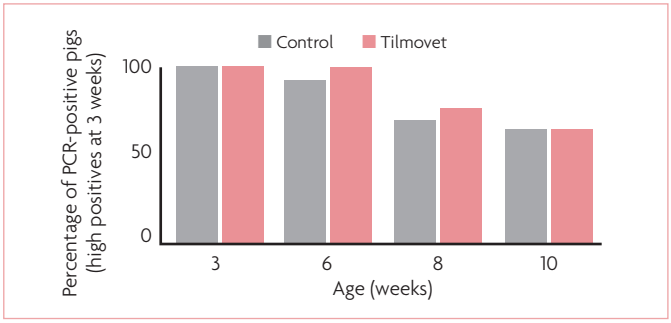


Fig. 5. Evaluation of the viral load of high positive piglets at study start, from the beginning to the end of the experimental trial (Spain study).

feed. Only a limited number of studies are published in which tilmicosin was administered via water to control PRRS infection after PRRSV inoculation or in naturally infected pigs post-weaning. The use of Tilmovet is an excellent strategy to stabilise PRRSV infection and to reduce the virus load during infection in PRRSV viraemia situations.

Tilmovet administration feed vs. water

Therapeutic Tilmovet can be given in feed. However, because sick pigs have a reduced appetite and variable feed intake, and because medicated feed may also take time to prepare and deliver, Tilmovet can be administered as a soluble formulation in drinking water.

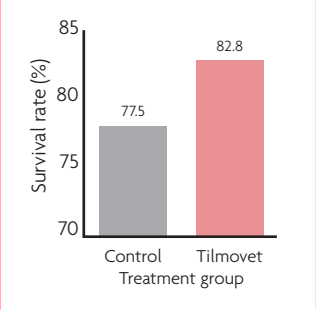
Based on the restrictions on using medicated premixes, veterinarians and pig producers often use Tilmovet water soluble as a highly effective alternative for disease management purposes.

PRRSV-positive herds post-weaning

The antiviral effect of Tilmovet Oral Solution in PRRSV viraemic pigs was determined in two field studies; one conducted in Taiwan and one in Spain.

The Taiwan study was conducted in a PRRSV-positive herd (Type 1 PRRSV strain) post-weaning with pigs aged 4-12 weeks.

Fig. 6. Survival rate age week 3 to 10 (Spain study).



In the herd, diverse pathogens (M. hyopneumoniae, A. pleuropneumoniae, G. parasuis, P. multocida) were present causing continuous respiratory problems post-weaning. 160 four-week old pigs were equally divided into four treatment groups (40 piglets/group).

Tilmovet Oral Solution was used in three different treatment programmes: Group 1: 5-day medication once (20mg/kg bw); Group 2: 5-days medication twice (15mg/kg bw) – with a 14 day medication stop in between; Group 3: 5-days medication three times (15mg/kg bw) – with a 14 day medication stop in between treatments; control Group 4: no treatment. Blood samples were randomly collected from 20 piglets in each treatment group at 4, 6, 8, 10 and 12 weeks of age for ELISA and qPCR testing.

PRRSV infection was found at 4 and 6 weeks of age at a low percentage of pigs in Group 1 (10%/15%), Group 2 (0%/5%) and Group 3 (0%, 25%) in comparison to the control pigs (30%/65%). The higher PRRSV burden in non-medicated control pigs resulted in higher PRRSV antibody levels (S/P ratios) over the whole trial period (see Figure 1). Tilmovet water medication led to a depression of PRRSV replication and consequently to lower ELISA antibody titres in the three medicated groups over the whole trial period.

Tilmovet treated pigs in Groups 2 and 3 exhibited a higher survival rate of 87.5% and 95% vs. 82.5% and a better weight gain of 0.380kg and 0.360kg in comparison to pigs in the control group (0.350kg).

The study in Spain was conducted in a transition farm which was affected by a PRRSV outbreak with the highly pathogenic Rosalia PRRSV strain. Animals on the farm were also affected by G. parasuis, M. hyopneumoniae post-weaning. 800 animals were divided into two treatment groups.

Tilmovet Oral solution was used in a 5-day medication programme three times (15mg/kg bw) with a 14 day medication stop in between and compared to a non-medicated control group. Blood samples for ELISA and qPCR determination and PRRSV clinical sigs were determined at 3, 6, 8 and 10 weeks of age.

A higher level of PRRSV PCR-positive pigs at study start (age week three) was determined in the control group (51.25%) and in the Tilmovet group (45.57%) in the Spain study compared to the Taiwan study.

To evaluate the effect of Tilmovet water medication in the Spain study, three subgroups were created according to the piglet's qPCR results (Ct value) at the enrolment of the study.

The three subgroups composed of those pigs that were negative to qPCR (Ct value >40), those that had low viral load at study entrance (Ct value between 30-40) and those animals with high viraemia on the day of the enrolment (Ct value <30).

In PCR-negative pigs at study start (three weeks of age) a positive effect of Tilmovet water medication was determined.

After the infection peak at six weeks of age the PRRS infection was reduced by 8% (week eight) and by 14% (week 10). In non-medicated pigs the percentage of positive pigs increased by 8% on week eight and by 5% on week 10.

Low level PCR-positive pigs at the beginning of the study in Tilmovet medicated group showed a higher infection reduction by 25% (six weeks of age) and by 47% at eight weeks of age vs. the control group, in which the viraemia decreased by 15% on age week six and 8% on age week eight.

In high level PCR-positive pigs at the beginning of the study, a similar infection reduction by 25% at eight weeks of age and 40% at 10 weeks of age in the Tilmovet group vs. the control group with 29% (eight weeks of age) and 40% (10 weeks of age) was found.

A higher survival rate at the study end was determined in the Tilmovet group (83%) in comparison to the control group (78%). Relatively low survival rates in both groups were based on the highly pathogenic PRRSV strain and the first disease outbreak caused by this strain on the Spanish farm. A higher daily weight gain was determined in pigs with Tilmovet water medication in comparison to the control group (see Table 2).

Conclusion

Tilmovet water medication in farms with low (Taiwan) and high (Spain) PRRSV infection levels shows a positive effect on PRRS clinical disease expression.

The high PRRSV infection reduction in the case of Tilmovet medication verify its stabilising effect of the PRRS infection situations in the presence of different respiratory bacteria pathogens. Implementation of Tilmovet water medication programmes after farrowing is a highly effective tool to control PRRS in PRRSV-viraemic herds with PRDC problems. ■

References are available from the author on request

Table 1. Body weight and average daily gain (ADG) of pigs in the four treatment groups (Taiwan study). [a],[b] indicate stat. sign. difference (p<0.05)

Age (weeks)	Group 1	Group 2	Group 3	Control
4	5.60	6.89	6.72	6.61
12	23.0	28.64	27.33	26.57
ADG (kg)	0.310[b]	0.380[a]	0.360	0.350

Table 2. Body weight and average daily gain (ADG) of pigs in the two treatment groups (Spain study).

Age (weeks)	Tilmovet (in kg)	Control (in kg)
3	5.56	5.30
10	19.47	17.97
ADG (kg)	0.30	0.27