VALNEMULIN ECONOR® PERFORMANCE

RESULTS FROM FIELD TRIALS AND CLINICAL STUDIES

NUMBER 8

ECONOR® PLUS CTC SHOWN TO BE EFFECTIVE FOR MIXED RESPIRATORY INFECTIONS IN SWINE

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INTRODUCTION

Respiratory infections in swine due to *Mycoplasma hyopneumoniae* can be costly for pork producers, but when other pathogens are present to complicate the picture, the economic impact escalates.

The causes of mixed respiratory infection differ, but one common combination of pathogens seen in the field is *M. hyopneumoniae*, *Pasteurella multocida* and *Actinobacillus pleuropneumoniae*. In some cases, *Haemophilus parasuis* and *Streptococcus suis* also may be involved.

Fortunately, mixed respiratory infections in swine can be controlled. Artificial infection studies and *in vitro* sensitivity testing indicate that a combination of Econor® (valnemulin), a new-generation pleuromutilin, and chlortetracycline (CTC) can provide effective treatment, which in turn can minimize the loss in performance and reduce the costs to pork producers.

Hungarian Studies

Researchers in Hungary tested the efficacy of Econor when used alone and in combination with CTC against *M. hyopneumoniae*, *P. multocida* and *A. pleuropneumoniae* and compared the results to those achieved with other antimicrobials.[1]

Table 1

Treatments administered in the Hungarian study.

Unmedicated Controls
Econor 25 mg/kg + CTC 400 mg/kg
Econor 75 mg/kg + CTC 400 mg/kg
Tiamulin 100 mg/kg + CTC 400 mg/kg
Tilmicosin (Pulmotil) 300 mg/kg

First they conducted *in vitro* studies with seven strains belonging to the species *M. hyopneumoniae*, *M. hyorhinis* and *M. hyosynoviae* to establish the minimum inhibitory concentration (MIC) for valnemulin and CTC.

Next, five groups of 10 pigs, each 5 to 6 weeks old, were infected with *M. hyopneumoniae* on Day 1, with *P. multocida* on Day 8 and with *A. pleuropneumoniae* on Day 15. One group was unmedicated and served as a control. From Days 9 to 21, pigs in the other four groups were treated with one of several feed antibiotic regimens — tilmicosin (Pulmotil®), tiamulin plus CTC or with Econor plus CTC in two different combinations as shown in the Table 1.

Investigators observed the pigs for clinical signs of disease and for the presence of lung lesions, while also measuring bodyweight gain and feed conversion ratios. They determined efficacy by utilizing immunofluorescence examination and attempting to reisolate pathogens in the lungs.

KEY POINTS

> Econor® plus CTC yielded significantly fewer gross lung lesions than tilmicosin in pigs with mixed respiratory infection at the dosages tested.

> The best feed conversion ratios and weight gain were seen in pigs treated with Econor and CTC compared to other antimicrobials tested.

> Econor plus CTC is effective against a broad spectrum of other respiratory pathogens seen in swine.

Results

> MICs against the tested mycoplasma strains were 0.0625 to 0.125 mcg/ml for valnemulin. This was lower than those for CTC, which were 1 to 8 mcg/ml.

> When valnemulin and CTC were combined, MIC values were even lower and, in fact, were 4 to 16 times lower than those of valnemulin or CTC alone.

> Gross lung lesion scores were significantly ($p<0.05$) better in the two groups that received Econor and CTC, compared to controls and the group that received tilmicosin.

> The best feed conversion ratios were seen in the two groups that received Econor and CTC.

> The two groups that received Econor and CTC also had significantly ($p<0.05$) less reisolation of mycoplasma pathogens from the lungs compared to controls and pigs that received tilmicosin.

> Weight gain was similar in all treated groups and was significantly ($p<0.05$) better than in controls, but the best weight gain was achieved with Econor plus CTC (Table 2).

Table 2

Artificial infection study results.

	Unmedicated Controls	Pulmotil 300	Tiamutin 100+ CTC 400	Econor 25+ CTC 400	Econor 75+ CTC 400
Gross lung lesion score	58	23	14*	8*+	6*+
Reisolation of MH	8/10	3/10*	0/10*+	0/10*+	0/10*+
Avg. weight gain days 9–21 (kg)	3.95	6.10*	6.00*	6.06*	6.17*
FCE days 9–21	2.91	1.72	1.75	1.73	1.69

* $p<0.05$ against unmedicated control.
+ $p<0.05$ against Pulmotil 300 ppm.

Researchers' observations: "The FCE was improved by the medications with valnemulin (Econor) 75 + CTC 400 giving the best performance."

Korean Study

MIC studies conducted in Korea, where mixed respiratory infections are a serious problem for swine producers, have confirmed results of the Hungarian studies.

Investigators tested the effectiveness of valnemulin alone and in combination with CTC against five swine respiratory pathogens: *M. hyopneumoniae*, *P. multocida*, *A. pleuropneumoniae*, *H. parasuis* and *S. suis*.[2] Multiple strains of each pathogen were included in the study and all of them were isolated in Korea. Other antimicrobials tested were tiamulin, lincomycin, tylosin and penicillin.

Results

> All strains of *M. hyopneumoniae* were susceptible to valnemulin at 0.0625 µg/ml to 0.0039 µg/ml.

> All strains of *M. hyopneumoniae* were the most susceptible to valnemulin and tiamulin.

> For all *M. hyopneumoniae* isolates tested, MIC values were from 4 to 8 times lower with valnemulin and CTC combined compared with valnemulin or CTC alone.

> A combination of valnemulin and CTC was active against all five bacteria species tested in the study (Table 3).

Bacteria	Tiamulin	Lincomycin	Penicillin	Valnemulin	CTC	Valnemulin/CTC
M. hyopneumoniae	0.031	0.25	–	0.031	0.125	0.0012-0.0049/ 0.0098-0.0195
A. pleuropneumoniae	16	32	4	16	1	1-8/ 0.0625-0.5
P. multocida	16	64	2	4	1	0.25-1/ 0.0625-0.25
H. parasuis	16	32	2	24	3	0.5-8/ 0.0625-1
S. suis	64	2048	0.55	8	8	0.5-8/ 0.5-2

Table 3

Synergistic efficacy of combinations of valnemulin and chlortetracycline for respiratory pathogens isolated in Korea.

Researchers' observations: "The combination of valnemulin and CTC showed good synergy against field isolates of five bacterial species."

Japanese Study

Studies with valnemulin and CTC alone and in combination for mixed infections also have been conducted in Japan, where researchers report that drug resistance to *P. multocida*, *A. pleuropneumoniae* and *B. bronchiseptica* is "a grave clinical problem."[3]

Investigators used several strains of recent clinical isolates in their studies. They determined MIC values and the effect of the drug combination was expressed as a Fractional Inhibitory Concentration (FIC) index. In addition, a standard time-killing curve method was used to study the interaction between valnemulin and CTC.

Results

> MICs for valnemulin ranged from 6.25 to 50 µg/ml for the three organisms tested and the potency of valnemulin against the three species was generally lower compared to that for CTC.

> The majority of strains – 51% – showed a synergistic effect and the remaining 49% showed an additive benefit when valnemulin and CTC were used together (Table 4).

Researchers' observations: "The results suggest that the combined use of valnemulin and CTC may be clinically useful in the treatment of respiratory tract infections in swine."

Organism	No. of Strains Used	No. of Strains (%) FIC Index ≤0.5 (Synergy)	No. of Strains (%) FIC Index >0.5~≤1 (Additive)
P. multocida	11	9 (82)	2 (18)
A. pleuropneumoniae	19	5 (26)	14 (74)
B. bronchiseptica	17	10 (59)	7 (41)
Total	47	24 (51)	23 (49)

Table 4

The results show the synergistic activity or an additive benefit of valnemulin combined with CTC.

" The two groups that received Econor and CTC also had significantly less reisolation of mycoplasma pathogens from the lungs…"

SUMMARY

Econor combined with CTC was shown to be significantly superior to tilmicosin for controlling *M. hyopneumoniae* at the dosages tested.

The combination of valnemulin plus CTC also has synergistic activity against a broad spectrum of other respiratory pathogens and should be useful for treating mixed respiratory infections in swine.

REFERENCES

[1]Stipkovits L, et al. The efficacy of combinations of Econor® + CTC, Tiamutin® + CTC in the treatment of piglets experimentally infected with *Mycoplasma hyopneumoniae*, *Pasteurella multocida* and *Actinobacillus pleuropneumoniae*. *The 15th International Pig Veterinary Society Congress*. 1998.

[2] Koh HB, et al. Efficacy of combinations of Econor® and chlortetracycline for *Streptococcus suis*, *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis* and *Mycoplasma hyopneumoniae* isolates in Korea. *The 16th International Pig Veterinary Society Congress*. 2000.

[3] Kitadai N, et al. *In vitro* combined effect of valnemulin with chlortetracycline against *P. multocida*, *A. pleuropneumoniae* and *B. bronchiseptica*. *The 15th International Pig Veterinary Society Congress*. 1998.

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