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# A comparison of tilmicosin to gamithromycin for on-arrival treatment of bovine respiratory disease in feeder steers

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## Abstract

A trial was conducted in a commercial feedlot in western Canada using fall-placed feedlot calves at moderate risk of bovine respiratory disease (BRD) to compare the efficacy of gamithromycin to tilmicosin for metaphylactic treatment of BRD. First-pull treatment rates for BRD were significantly lower ($P = 0.01$) in calves in the gamithromycin group than in the tilmicosin group. There were no other significant differences in health or performance between the two groups. The 6.6 percentage point difference in treatment rates for BRD equated to a net advantage of $0.03CAN/head for those calves given gamithromycin as a metaphylactic drug on arrival compared to metaphylactic treatment with tilmicosin. Drug cost and disease risk should be carefully evaluated in each feedlot and group of incoming cattle to determine the most cost-effective metaphylaxis protocol.

**Key words:** gamithromycin, tilmicosin, metaphylaxis, bovine respiratory disease

## Résumé

Un essai a été mené dans un parc d'engraissement commercial de l'ouest du Canada avec des veaux de parc arrivés en automne avec un risque modéré pour les maladies respiratoires bovines afin de comparer l'efficacité de la gamithromycine et de la tilmicosine pour le traitement prophylactique des maladies respiratoires bovines. Le taux de premier traitement pour les maladies respiratoires bovines était significativement moins élevé (P = 0.01) dans le groupe recevant la gamithromycine plutôt que la tilmicosine. Il n'y avait aucune autre différence au niveau de la santé et de la performance entre les deux groupes. La différence de 6.6% dans le taux de traitement pour les maladies respiratoires bovines représentait l'équivalent d'un avantage net de 0.03$ CAN par tête pour les veaux traités prophylactiquement avec la gamithromycine plutôt qu'avec la tilmicosine à leur arrivée. Le coût du traitement et le risque de maladie devraient être évalués avec soin dans chaque parc d'engraissement et dans chaque groupe de bétail afin de déterminer le protocole de prophylaxie le plus rentable.

## Introduction

Metaphylactic antimicrobials are used in moderate to high disease-risk calves to reduce morbidity and mortality from bovine respiratory disease (BRD) and to improve performance.[8,12] Drugs currently used metaphylactically to control BRD in recently weaned feedlot calves in western Canada are long-acting oxytetracycline, tilmicosin,[a] and tulathromycin.[b] Numerous published field trials demonstrate the efficacy of these antimicrobials in reducing BRD.[1,8,9,12,13]

Gamithromycin[c] was recently licensed in Canada. Gamithromycin is a novel azalide developed for treatment and prevention of BRD.[3,5,6,10,11] It belongs to the macrolide family of antibiotics and is characterized by having low serum concentrations, high tissue concentrations, and extended tissue elimination half-life.[5] To date, there are no published, large-scale controlled field trials conducted in commercial feedlots in North America to demonstrate the efficacy of gamithromycin to control BRD, nor are there any comparative studies to other metaphylactic drugs to demonstrate its cost effectiveness.

The purpose of this controlled field trial was to evaluate the effectiveness of tilmicosin administered on arrival compared to gamithromycin administered on arrival for reducing morbidity and mortality due to naturally occurring BRD in a commercial feedlot. The second objective was to compare performance (average daily gain (ADG) and dry matter conversion (DMC)) of calves administered tilmicosin or gamithromycin on arrival.

## Materials and Methods

*Study Facility*

This study was conducted at a commercial feedlot in southern Alberta, Canada with a one-time feeding capacity of 25,000 head. The animals were housed in

open dirt-floor pens with a heated automatic waterer and a concrete feed bunk within the fence line facing a common feed alley. Each pen held 250 animals on average. The hospital and treatment areas at the feedlot were used to manage sick cattle. The hospital has a roof and concrete floor and is equipped with a hydraulically operated squeeze chute with weigh scale and chute-side computer and health data management system.[d] Body temperatures were taken with an electronic thermometer.

Cattle were fed rations consisting of barley grain, barley or corn silage, corn dried distiller grains with solubles, and supplement formulated to meet standard nutritional requirements of feedlot cattle. Monensin sodium[e] was included in the ration throughout the feeding period to improve performance and control bloat and coccidiosis. Chlortetracycline was fed in the starter ration to control histophilosis. Cattle were fed ration three times daily on an ad libitum basis using truck-mounted mixers on load cells. Feed intake was recorded by pen, with feed from sick and chronic pens prorated back to the original lot of cattle.

*Study Animals*

Five thousand crossbred steer calves six to 10 months of age, with an average weight of 686 lb (312 kg), were used in the study. All animals had been recently purchased through the auction market system or direct from ranches and shipped to the feedlot.

Upon arrival at the feedlot, animals were given a modified-live infectious bovine rhinotracheitis (IBR) and bovine viral diarrhea (types 1 & 2) vaccine, 8-way clostridial bacterin, *Histophilus somni* bacterin, *Mannhemia haemolytica* leukotoxin vaccine, ivermectin pour-on or injectable, and an anabolic growth implant. If it was raining or wet snow, animals within a processing group were treated with an injectable ivermectin rather than pour-on ivermectin. Animals were re-vaccinated with a modified live IBR-parainfluenza-3 vaccine and they received a terminal growth promoting implant at approximately 70 days-on-feed (DOF). The implant program was consistent across all pens. All animals were uniquely identified with a numbered feedlot eartag and Canadian Cattle Identification Agency tag. Animals were put onto the study within 48 hours after arrival at the feedlot.

*Experimental Design*

A randomized block design was used. Each block consisted of two pens as they were filled. A total of 20 pens or 10 blocks were created. The sample size used is typical for commercial feedlot trials when assessing metaphylactic drugs or feed additives, and the pen was the unit of analysis.[1,13]

The two treatments were: 1) gamithromycin administered subcutaneously at 2.72 mg/lb (6 mg/kg) of body weight, and 2) tilmicosin SC at 4.54 mg/lb (10 mg/kg) of body weight. Both drugs were administered at arrival regardless of rectal temperature, and no other metaphylactic antimicrobials were given. On-arrival treatments were dosed according to the average weight of animals in that processing group.

Animals administered gamithromycin were not eligible for additional therapy until 10 days following on-arrival treatment (post-metaphylactic interval [PMI]). The 10-day PMI was based on the Canadian label claim and previous pharmacokinetic information provided in the literature.[3,5] Animals administered tilmicosin were not eligible for additional therapy until five days following on-arrival treatment (5 day PMI), the standard PMI used for tilmicosin at this feedlot. Moribund animals were euthanized for humane reasons, regardless of days post-metaphylaxis.

All animals pulled for treatment for BRD were treated according to the feedlot's standard treatment protocol for BRD. Animals relapsing a third time with BRD were considered chronics; thus, no further treatment was given and they were placed in a chronic pen. Therapeutic drugs were used at label dose with label withdrawals adhered to. Treatment dosages were based on the individual body weight of the sick animal.

*Animal Allotment*

Experimental animals were selected from large groups of animals arriving at the feedlot from October 18 to November 30, 2010. As new cattle were presented for processing, calves within each arrival processing group were randomly assigned to one of two treatment groups using systematic randomization. A coin was flipped to determine which of the feeding pens was used to house cattle treated with tilmicosin or gamithromycin. Then a coin was flipped to determine if the first calf through the chute for a new block of pens went into the tilmicosin or gamithromycin group. Every other animal through the chute went into the same treatment group. For example, if the coin flip was heads and heads was set for tilmicosin, then the first calf through the chute received tilmicosin, the second calf through the chute received gamithromycin, the third calf through the chute received tilmicosin, and so on until pens were filled.

Calves were processed and individually weighed in the processing chute. The scale in the processing chute was verified with a standard weight and calibrated as necessary prior to processing. After every 20 head, the scale was tared to zero. Calves from the two treatment groups were penned separately. Once two pens were full (250 animals each) two new pens were filled until 20 pens were placed on trial. Each pen was an experimental unit and each group of two pens represented a block. Animals were moved to their home pen and maintained as a unit for the duration of the trial, which

was from induction processing until terminal weight sorting (approximately 30 to 40 days before slaughter). Feedlot personnel who processed the cattle were different from feedlot personnel who checked the cattle daily for illness. The trial could not be blinded because the health crew (i.e. pen riders) needed to know the PMI of the cattle to determine when sick animals could be pulled and treated for BRD.

*Observations*

Any animals appearing "sick" based on subjective parameters, such as general appearance and attitude, gauntness, reluctance to move, or separation from group, were moved to the hospital area of the feedlot for closer observation. Upon presentation at the hospital facility, the rectal temperature of the "sick" calf was taken with an electronic thermometer and its identification entered into the chute-side computer.[d]

A diagnosis of the initial case of BRD was made on an animal if the following criteria were satisfied: 1) the case abstract, which appeared on the computer screen, indicated no previous treatment history for BRD; 2) there was an absence of clinical signs referable to organ systems other than the respiratory tract; and 3) animals meeting the temperature criteria ($\geq$ 104.0°F or 40°C). If all criteria were met, the animal was treated and designated as undifferentiated fever (UF). Animals not meeting the temperature criteria were treated and designated as no fever (NF). All treated animals (UF and NF) were returned to their home pen the same day of treatment unless they were overly compromised. Cattle with compromised mobility were housed in the hospital pen until they could be returned home.

A diagnosis of a relapse case of BRD was made if the following criteria were satisfied: 1) the case abstract indicated previous treatment for BRD (UF or NF) and 2) there was an absence of clinical signs referable to organ systems other than the respiratory tract. If treatment for BRD was necessary, then animals were treated according to the feedlot's standard treatment protocol.

A calf was defined as a chronic if it had been pulled as a third relapse; these animals were sent to the chronic pen. If calves were moribund at any time, they were humanely euthanized. Calves that were gaining weight but could not be returned to their home pen because they could not compete with their peers for feed or water were sent to a rail pen for fattening for salvage harvest; else, they were euthanized.

Animals that died during the trial period were necropsied by the feedlot veterinarians to determine the cause of death.

*Statistical Analysis*

The following data were analyzed on a pen basis from arrival to terminal weight sort: 1) BRD initial treatment rate (UF0 and NF0); 2) BRD first relapse rate (UF1 and NF1); 3) BRD second relapse rate (UF2 and NF2); 4) BRD chronicity rate (UF3 and NF3); 5) crude mortality rate; 6) mortality rate for BRD and histophilosis; 7) weight gain; 8) ADG; 9) daily dry matter intake (DDMI); 10) DMC; and 11) DOF.

Individual body weights at processing, reimplant, and terminal weight sort were imported into a spreadsheet program,[f] and the average weight was calculated for each pen. From the computerized animal health data, proportional rates for BRD treatment, overall mortality, and BRD/histophilus mortality were calculated for each pen. Histophilus mortality included death from myocarditis, pericarditis, pleuritis, and arthritis.

Body weights, DOF, DDMI, ADG, and DMC were calculated for each pen at first implant and at terminal weight sort. Reimplant and terminal weight sort body weights were shrunk 4%, which is the standard industry practice of reducing chute weights by 4% to account for animal weight attributed to gut fill. Weight gain per pen was the change in average weight from induction to terminal weight sort. Average DOF per pen was calculated as the total head days divided by the number of head inducted, ADG per pen was calculated as the reimplant or terminal sort weight minus the total weight inducted, divided by the total head days. DDMI per pen was calculated as the total pounds of feed fed divided by total head days. DMC per pen was calculated as the total pounds of feed fed divided by total weight gain.

Data were analyzed using an analytical software program.[g] A randomized complete block analysis of variance was used to compare outcomes between experimental groups. Statistical significance was set at $P \leq 0.05$.

The relative cost-effectiveness of the metaphylactic drugs was calculated based only on health and performance variables that were statistically different between the two experimental groups. Variables included the current metaphylactic antimicrobial therapy costs of $16.48CAN for gamithromycin and $14.61CAN for tilmicosin, an initial BRD therapy cost of $27.82CAN per animal, plus a $1CAN per animal labor charge for pulling and treating BRD cases.

## Results and Discussion

First-pull treatment rates for BRD were significantly lower in the gamithromycin group than in the tilmicosin group (Table 1). There were no other significant differences in health or performance (Table 2) between treatment groups. The overall disease rates may have been lower in both groups due to the feeding of chlortetracycline to reduce morbidity and mortality from histophilosis. This may have reduced our ability to see treatment differences in relapses or mortality. It is typical in many western Canadian feedlots to feed

**Table 1.** Effect of on-arrival treatment with tilmicosin or gamithromycin on morbidity and mortality of feedlot steer calves at moderate risk for BRD.

| Variable | Experimental Group | | SEM | *P*-value |
|---|---|---|---|---|
| | Tilmicosin[a] | Gamithromycin[b] | | |
| No. pens | 10 | 10 | | |
| No. animals | 2500 | 2500 | | |
| First BRD (UF+NF) treatment (%) | 20.2 | 13.6 | 1.5 | 0.01 |
| First UF[c] treatment (%) | 19.2 | 12.8 | 1.3 | 0.008 |
| First NF[d] treatment (%) | 1.0 | 0.8 | 0.2 | 0.37 |
| First BRD relapse (%) | 16.3 | 13.0 | 1.8 | 0.22 |
| First UF relapse (%) | 16.9 | 13.7 | 1.8 | 0.25 |
| First NF relapse (%) | 5.0 | 0 | 3.5 | 0.34 |
| Second BRD relapse (%) | 9.2 | 8.1 | 3.5 | 0.83 |
| Second UF relapse (%) | 9.3 | 8.1 | 3.5 | 0.81 |
| Second NF relapse (%) | 0 | 0 | NA | 1.0 |
| Third BRD relapse (%) | 10.0 | 0 | 7.1 | 0.34 |
| Third UF relapse (%) | 10.0 | 0 | 7.1 | 0.34 |
| Total mortality (%) | 0.9 | 1.3 | 0.2 | 0.10 |
| BRD/histophilus mortality (%) | 0.4 | 0.6 | 0.1 | 0.14 |

[a]Micotil®, Elanco Animal Health, Guelph, Ontario, Canada
[b]Zactran®, Merial Canada Inc., Baie Durfe, Quebec, Canada
[c]UF = undifferentiated fever
[d]NF = no fever

**Table 2.** Effect of on-arrival treatment with tilmicosin or gamithromycin on performance of feedlot steer calves at moderate risk for BRD.

| Variable | Experimental Group | | SEM | *P*-value |
|---|---|---|---|---|
| | Tilmicosin[a] | Gamithromycin[b] | | |
| No. pens | 10 | 10 | | |
| No. animals | 2500 | 2500 | | |
| Induction weight (lb) | 686 | 686 | 0.68 | 0.84 |
| DOF[c] at first reimplant | 69 | 69 | 0.09 | 0.17 |
| 1st reimplant weight (lb) | 881 | 886 | 2.22 | 0.11 |
| DDMI[d] at 1st reimplant (lb) | 15.4 | 15.7 | 0.18 | 0.28 |
| ADG[e] at 1st reimplant (lb/day) | 2.71 | 2.72 | 0.05 | 0.86 |
| DMC[f] at 1st reimplant | 6.29 | 6.33 | 0.12 | 0.78 |
| DOF at terminal sort | 192 | 192 | NA | 1.0 |
| Terminal sort weight (lb) | 1284 | 1282 | 5.73 | 0.82 |
| Weight gain (lb) | 598 | 596 | 5.90 | 0.84 |
| Terminal wt sort DDMI (lb) | 19.1 | 19.0 | 0.07 | 0.34 |
| Terminal wt sort ADG (lb) | 3.08 | 3.04 | 0.03 | 0.43 |
| Terminal wt sort DMC | 6.52 | 6.63 | 0.07 | 0.31 |

[a]Micotil®, Elanco Animal Health, Guelph, Ontario, Canada
[b]Zactran®, Merial Canada, Inc., Baie Durfe, Quebec, Canada
[c]DOF = days-on-feed
[d]DDMI = daily dry matter intake
[e]ADG = average daily gain
[f]DMC = dry matter conversion

chlortetracycline in starter rations to reduce morbidity and mortality from histophilosis.

Another factor which may have affected treatment response rates in both groups is dosing the metaphylactic drug based on the average induction weight of each incoming processing group. Thus, some individual cattle may have received more drug than the label dose, which may have provided no additional health benefits. Other cattle may have been under dosed, potentially reducing treatment response. Given that the dose of the metaphylactic drug was averaged in both treatment groups, it is unlikely that there was any directional bias favoring one drug over the other. It is typical in large commercial feedlots which process over 100 head of cattle per hour to base the dose of the metaphylactic drug on the average arrival weight of the incoming group of calves. At this feedlot, calves are bought in 100 lb (45.5 kg) weight groups; therefore, the variability in incoming weight within a processing group of calves is typically not very large, suggesting that averaging the dose of the metaphylactic drugs within each processing group most likely had little effect on overall treatment responses.

The lower first-pull BRD treatment rates in the gamithromycin group may be due to differences in the pharmacokinetics of gamithromycin compared to tilmicosin, including its elimination half-life and distribution to lung tissue.[5,7] It may also be due to the shorter PMI imposed on the tilmicosin treated cattle in this study, which could have reduced the treatment success rate for tilmicosin. Cattle which may have recovered on their own if given more time may have been prematurely repulled and retreated in the tilmicosin group. A five-day PMI was used for tilmicosin since it was the standard PMI used for the drug in this feedlot. Previous work has suggested that the PMI for tilmicosin can be extended from three to seven days, improving treatment success rates.[2]

The health crew was not blinded to the metaphylactic treatments because of the different PMI set for each drug. It is not known if this lack of blinding created any directional bias in the results. Gamithromycin was a new drug on the market and the crew had never heard of or used it previously, so it is unlikely that the crew, which were experienced pen riders, had any preconceived views on its efficacy that could have biased repull rates.

Additional studies should be conducted comparing the two drugs with no PMI or the same PMI. As well, additional studies should be conducted in different disease-risk calves, and the studies should be followed through from arrival to harvest and include carcass data.

The unit of analysis in this study, the pen, could not be maintained as a unit from arrival until harvest. This study was discontinued at terminal weight sorting due to mixing of cattle into different pens prior to sale to reduce overweight and underweight carcasses. However, it is unlikely that following the cattle through to harvest would have changed the health or performance outcomes given that most BRD occurred early in the feeding period and any performance differences, if not observed at terminal weight sort, are unlikely to occur later on in the feeding period. It is unknown whether there were differences in carcass traits between the treatment groups. Typically, differences in carcass data are only observed in cattle with BRD following multiple treatments for BRD (chronics) and when there are also significant performance differences observed.[4] There were no differences in BRD relapse rates between treatment groups and no differences in performance; therefore, it is unlikely that there would have been differences in carcass traits if the cattle had been followed through to harvest.

The 6.6% difference in treatment rates equated to a $1.90CAN/head greater (0.066 x $28.82/head) first-pull BRD treatment cost for tilmicosin cattle than for gamithromycin cattle. When the difference in the cost of metaphylaxis was included ($1.87CAN/head) in the economic calculation, the net advantage was $0.03CAN/head for those calves administered gamithromycin as a metaphylactic drug on arrival as compared to tilmicosin. At the time the study was conducted in 2010, there was a net economic advantage of $10.19CAN/head for the tilmicosin group due to the higher purchase price of gamithromycin and the lower cost of the first therapeutic drug used to treat BRD. The current small difference in cost-effectiveness of these two metaphylactic drugs suggests that practicing veterinarians should regularly evaluate the costs and efficacy of various drugs. Based on current treatment costs and health response differences in differing disease-risk cattle, bovine practitioners can determine which drugs are most cost-effective for their feedlot clients at any given time.

## Conclusion

Metaphylactic treatment with gamithromycin reduced first-pull treatments by 6.6 percentage points compared to treatment with tilmicosin in fall steer calves at moderate risk of BRD. However, drug costs and disease risks need to be evaluated carefully on a case-by-case basis in each feedlot to determine the most cost-effective metaphylactic protocol.

## Endnotes

[a]Micotil®, Elanco Animal Health, Division of Eli Lilly Canada Inc., Guelph, Ontario, Canada
[b]Draxxin®, Pfizer Animal Health, Pfizer Canada Inc., Kirkland, Quebec, Canada
[c]Zactran®, Merial Canada Inc., Baie Durfe, Quebec, Canada

[d]DG Pro, Computer Aid, Okotoks, Alberta, Canada
[e]Rumensin Premix, Elanco Animal Health, Division of Eli Lilly Canada Inc., Guelph, Ontario, Canada
[f]Microsoft® Office Excel®, Microsoft Corporation, One Microsoft Way, Redmond, WA
[g]Statistix 8 Analytical Software, Tallahassee, FL


## Acknowledgements

We thank the management and staff at the participating feedlot and Kerry Hyatt for her assistance in data collection. The project was funded by Elanco, a Division of Eli Lilly Canada, Inc.


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