

# Comparison of gamithromycin and tildipirosin for metaphylaxis treatment of winter-placed feedlot calves for control of bovine respiratory disease

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## Abstract

A randomized complete-block design trial was conducted in a commercial finishing feedlot in southern Alberta, Canada using winter-placed heifer calves ( $n = 4574$ ; initial body weight  $672 \pm 43$  lb;  $305.5 \pm 19.5$  kg) to evaluate the comparative efficacy of metaphylactic treatment with gamithromycin or tildipirosin for control of bovine respiratory disease. There were no statistically significant differences ( $P > 0.05$ ) in health or feedlot performance between calves treated with gamithromycin or tildipirosin from arrival to terminal weight sort, approximately 30 days before slaughter. Using current drug prices, metaphylactic treatment with gamithromycin had a net economic advantage of \$4.13CAN/head to those treated with tildipirosin on arrival.

**Key words:** bovine respiratory disease, BRD, feedlot, metaphylaxis treatment

## Résumé

Un essai randomisé à blocs complets a été mené dans un parc d'engraissement commercial du sud de l'Alberta (Canada) avec des veaux femelles placés en hiver ( $n = 4574$ ; poids initial  $672 \pm 43$  lb;  $305.5 \pm 19.5$  kg) afin d'évaluer l'efficacité relative d'un traitement métaphylactique avec soit de la gamithromycine ou soit de la tildipirosine pour contrôler le complexe respiratoire bovin. Il n'y avait pas de différence statistiquement significative ( $P > 0.05$ ) entre les deux traitements pour la santé et pour la performance d'engraissement de l'arrivée jusqu'au tri terminal par le poids approximativement 30 jours avant l'abattage. En utilisant le prix courant des drogues, il y aurait un avantage économique de 4.13\$ Can par tête à utiliser la gamithromycine plutôt que la tildipirosine à l'arrivée.

## Introduction

Various metaphylactic antimicrobials, such as long-acting oxytetracycline, tilmicosin, tulathromycin, tildipirosin, gamithromycin, and ceftiofur crystalline free acid, are commonly used in fall-placed feedlot calves to reduce morbidity and mortality from bovine respiratory disease (BRD), and to improve performance.<sup>1,2,3,6,8,9,10,11,13,14,15,16,17</sup> There is limited data on the comparative efficacy of metaphylactic antimicrobials in winter-placed backgrounded calves to control BRD in commercial feedlots in North America.<sup>9,15</sup>

The purpose of this controlled field trial was to evaluate the comparative effectiveness of gamithromycin to tildipirosin administered on arrival to winter-placed backgrounded calves in reducing morbidity and mortality due to naturally occurring BRD in a commercial feedlot. Secondary objectives were to measure performance (average daily gain and dry matter conversion) of calves administered gamithromycin or tildipirosin on arrival, and to calculate the comparative cost benefit of the 2 antimicrobials.

## Materials and Methods

### Study Facility

This study was conducted at a commercial feedlot in southern Alberta, Canada with a one-time feeding capacity of 14,000 head. The cattle 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 approximately 230 animals. The hospital and treatment area was used to administer treatments and weigh animals. The hospital had a roof and concrete floor, and was equipped with a hydraulically operated squeeze chute with weigh scale and chute-side computer and health data management system.<sup>a</sup> Body temperatures were taken with an electronic thermometer.<sup>b</sup>

Cattle were fed rations consisting of barley grain, barley or corn silage, corn dried distiller grains with solubles, and supplement formulated to meet nutritional requirements of feedlot cattle, consistent with normal feeding protocols in the feedlot. Monensin sodium<sup>c</sup> (33 ppm, 100% dry-matter basis) was included in the ration throughout the feeding period to improve performance and control bloat and coccidiosis. Tylosin phosphate<sup>d</sup> (11 ppm, 100% dry-matter basis) was included in the ration throughout the feeding period to reduce liver abscesses. All pens were fed 3 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. The dry-matter (DM) content of the ration varied from starter rations (approximately 55% DM) to finishing rations (approximately 77% DM).

### Study Animals

A total of 4,574 crossbred heifer calves approximately 7 to 9 months of age with an average induction weight of 672 lb (305 kg) were used in the study. All calves had been recently purchased through the auction market system and shipped to the feedlot. These were winter-placed calves that had been weaned the previous fall and then backgrounded either in another feedlot or on the ranch. The previous history of the calves was not known since that information is not typically provided to finishing feedlots in Alberta.

Upon arrival at the finishing feedlot, calves were given a modified-live virus infectious bovine rhinotracheitis and bovine viral diarrhea type 1 and 2 vaccine,<sup>e</sup> combination 8-way clostridial bacterin + *Histophilus somni* bacterin,<sup>f</sup> *Mannheimia haemolytica* leukotoxoid vaccine,<sup>g</sup> ivermectin pour-on or injectable,<sup>h,i</sup> and an anabolic growth-promoting implant.<sup>j</sup> If it was raining or wet snow was falling, animals within a processing group were administered injectable ivermectin rather than pour-on ivermectin. All animals were uniquely identified with a numbered feedlot eartag and Canadian Cattle Identification Agency tag. Animals were on the study within 48 hours after arrival at the feedlot. Cattle were reimplanted<sup>k</sup> at 80 to 90 days-on-feed (DOF).

### Experimental Design

A randomized block design was used. Each block consisted of 2 pens as they were filled, creating a total of 20 pens or 10 blocks. The sample size used in the study is typical for commercial feedlot trials when assessing metaphylactic drugs or feed additives, and the pen was the unit of analysis.<sup>15,16,17</sup>

The 2 arrival study treatments were: 1) gamithromycin<sup>l</sup> (GAM) administered SC at 2.7 mg/lb (6 mg/kg) of body weight and 2) tildipirosin<sup>m</sup> (TIL) administered SC at 1.8 mg/lb (4 mg/kg) of body weight. Gamithromycin or tildipirosin were administered at arrival regardless of body temperature, and no other metaphylactic antimicrobials were given. On-arrival

metaphylactic treatment was dosed according to the average weight of animals in each processing group. The weight range within processing groups was typically 100 lb (45.5 kg). Given that the 2 metaphylactic drugs were licensed and approved pharmaceuticals in Canada and both were used as per label directions, with the feedlot operating according to its normal management practices, there was no requirement for government approval to conduct the study.

Animals administered GAM or TIL were not eligible for additional therapy until 5 days following on-arrival treatment, i.e., 5-day post-metaphylactic interval (PMI). This was the standard PMI used for both study drugs at this feedlot. Because there is no published data defining the optimal PMI for TIL or GAM, the same PMI was used for each treatment.

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

### Animal Allotment

Experimental animals were selected from large groups of animals arriving at the feedlot from February 05 to March 24, 2016. As new cattle were presented for processing, calves within each arrival processing group were randomly assigned to 1 of 2 treatment groups using systematic randomization in groups of 5 head. A coin was flipped to determine which of the feeding pens would house GAM- or TIL-treated cattle. Then a coin was flipped to determine if the first calf through the chute for a new block of pens was assigned to either the GAM or TIL treatment group. Every group of 5 consecutive animals through the chute were assigned to the same treatment group. For example, if the coin flip was heads and heads was set for GAM, then the first 5 calves through the chute received GAM, the second 5 calves through the chute received TIL, the next 5 calves through the chute received GAM, and so on until the 2 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; the scale was tared to zero after every 20 head. Treatment groups were penned separately. Once 2 pens were full (approximately 230 animals in each pen), 2 new pens were filled until 20 pens of calves were enrolled in the trial. Pen was the experimental unit, and each group of 2 pens represented a block. Following processing, calves 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 days before slaughter). Feedlot personnel that processed the cattle were different from those that checked the cattle daily for signs of illness.

## Observations

Any animals appearing “sick” based on subjective parameters such as general appearance and attitude, gauntness, reluctance to move, separation from group, and signs of respiratory disease, such as nasal discharge, ocular discharge, abnormal respiration, and coughing, were removed from the pen and moved to the hospital area of the feedlot. Upon presentation at the hospital facility, the rectal temperature of the calf was taken with an electronic thermometer<sup>b</sup> and its identification entered into the chute-side computer.<sup>a</sup>

A diagnosis of the initial case of UF (Undifferentiated Fever) 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 (UF or NF); 2) there was an absence of clinical signs attributable to organ systems other than the respiratory tract as described above; and 3) animals met the temperature criteria ( $\geq 104.0^{\circ}\text{F}$ ;  $40^{\circ}\text{C}$ ). If all these criteria were met then the animal was treated and designated as UF. Animals with clinical signs of BRD and a rectal temperature of  $< 104^{\circ}\text{F}$  ( $40^{\circ}\text{C}$ ) were treated and designated as NF (No-Fever). All BRD treated animals (UF and NF) were returned to their home pen the same day of treatment unless they were severely compromised. Cattle severely compromised were housed in the hospital pen until they could be returned to their home pens.

Calves were considered a relapse (UF or NF) 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 attributable to organ systems other than the respiratory tract. Calves were classified as a relapse if repulled for BRD at any time while on feed, regardless of the time interval from the previous treatment. Calves that relapsed were treated according to the feedlot's standard treatment protocol for UF or NF, regardless of experimental treatment.

A calf was defined as a chronic if it was pulled as a third relapse, and sent to the chronic pen. Moribund calves were humanely euthanized, regardless of DOF. Calves gaining weight but could not be returned to their home pen because they could not compete with peers for feed/water were sent to a railer pen for fattening prior to slaughter. Feed from these cattle was prorated back to their home pen. The feedlot veterinarians necropsied all calves that died during the study to determine the cause of death.

### Statistical Analysis

Equations used to calculate morbidity and mortality rates have been previously defined.<sup>17</sup> Bovine respiratory disease cases included both UF and NF. Individual body weights at processing and terminal implant were imported into a spreadsheet program<sup>n</sup> and an average weight was calculated for each pen. From the computerized animal health data, disease rates for UF, NF, BRD (UF + NF), ART (arthritis),

and crude and case-specific BRD/*Histophilus somni* (BRDHS) mortality<sup>14</sup> were calculated for each pen. Arthritis cases were animals that were lame with 1 or more swollen joints. BRD/*Histophilus somni* mortality included fibrinous pneumonia, bronchopneumonia, pleuritis, myocarditis, pericarditis, and arthritis.

Terminal implant weight, DOF, daily dry matter intake (DDMI), average daily gain (ADG), and dry matter conversion (DMC) were calculated for each pen. Terminal implant weights were pencil shrunk using the industry standard of 4%. Average DOF per pen was calculated as the total head days divided by the number of head inducted. Average daily gain per pen was calculated as the difference between the total final ship weight and the total induction weight divided by the total head days. Daily DMI per pen was calculated as the total pounds of feed fed divided by the total head days. Dry matter conversion per pen was calculated as the total pounds of feed fed divided by the total live-weight gain. Feedlot performance was calculated with the weight of dead animals removed from the total final ship weight.

Data were analyzed using an analytical software program.<sup>o</sup> A randomized block design was used to compare outcomes between experimental groups. Linear regression models were used to evaluate continuous outcomes, and logistic regression models were used to compare proportional outcomes such as morbidity and mortality risk. A  $P < 0.05$  was considered statistically significant.

The relative cost effectiveness of the metaphylactic drugs was calculated based on health and performance variables that were statistically different between the 2 experimental groups. Variables that were not statistically significant were not included in the economic calculation.

## Results and Discussion

There were no statistically significant differences ( $P > 0.05$ ) in BRD (UF, NF) or arthritis, first pull and relapse rates, or total mortality and BRD/*Histophilus somni* mortality between the 2 treatment groups (Table 1). There were no significant differences ( $P > 0.05$ ) in ADG, DDMI, DMC or body weight between the 2 treatment groups (Table 2). The disease rate for BRD was low in these calves after the metaphylactic antimicrobials were given. Failure to see a difference in treatment groups may have been due to a low BRD disease rate, although these low BRD disease rates are what we anticipate after administration of an effective metaphylactic antimicrobial. Disease rates in winter-placed calves in feedlots in southern Alberta can be highly variable, and are typically much higher without metaphylactic antimicrobials.<sup>16</sup>

A 5-day PMI was used for calves in both study groups since it was the standard PMI used for these drugs at the study feedlot. It is unknown if changing the PMI for either drug would affect health or performance differences between treatment groups. There is no published data to indicate

**Table 1.** Comparison of gamithromycin and tildipirosin metaphylaxis on morbidity and mortality in winter-placed feedlot heifer calves at moderate risk of developing bovine respiratory disease (BRD).

Health variable	Experimental group		RR (95% CI)	P-value
	Gamithromycin*	Tildipirosin**		
No. of pens	10	10		
No. of animals	2287	2287		
First BRD (UF+NF) treatment, %	5.6	4.7	1.2 (0.91-1.48)	0.23
First UF*** treatment, %	5.0	4.3	1.2 (0.88-1.49)	0.30
First NF <sup>†</sup> treatment, %	0.56	0.44	1.3 (0.57-2.93)	0.53
First BRD (UF+NF) relapse, %	20.3	14.9	1.4 (0.79-2.60)	0.23
First UF relapse, %	22.9	15.6	1.5 (0.80-2.69)	0.22
First NF relapse, %	5.0	5.0	1.0 (0.06-15.3)	0.99
Second BRD (UF+NF) relapse, %	38.9	23.3	1.7 (0.32-1.67)	0.42
Second UF relapse, %	38.9	23.3	1.7 (0.32-1.67)	0.25
Second NF relapse, %	0	0	—	—
Third BRD (UF+NF) relapse, %	0	0	—	—
Third UF relapse, %	0	0	—	—
Third NF relapse, %	0	0	—	—
First ART <sup>‡</sup> treatment, %	1.2	1.5	0.8 (0.48-1.31)	0.37
First ART relapse, %	4.0	7.0	0.6 (0.04-1.64)	0.57
Crude mortality, %	0.70	0.57	1.2 (0.59-2.53)	0.56
BRDHS <sup>‡</sup> mortality, %	0.26	0.26	1.0 (0.32-3.06)	0.99
Removals, %	0.87	0.66	1.3 (0.47-2.86)	0.96

\*Zactran®, Merial Canada, Baie-D'Urfe, Quebec

\*\*Zuprevo™, Merck Animal Health, Intervet Canada Corp., Kirkland, Quebec

\*\*\*UF = undifferentiated fever

†NF = no fever

‡ART = arthritis

‡BRDHS = bovine respiratory disease and *Histophilus somni* disease

**Table 2.** Comparison of gamithromycin versus tildipirosin metaphylaxis on feedlot performance of winter-placed feedlot heifer calves at moderate risk of developing bovine respiratory disease.

Health variable	Experimental group		SEM	P-value
	Gamithromycin*	Tildipirosin**		
No. head/pen	229	229	3.75	1.00
Avg arrival weight, lb	672	671	2.13	0.71
Avg terminal sort weight, lb***	1,247	1,248	4.38	0.94
Avg weight gain, lb	575	577	5.31	0.63
DOF <sup>†</sup>	186	186	0.00	1.00
DDMI <sup>‡</sup> , lb	21.5	21.6	0.06	0.11
ADG <sup>‡</sup> , lb/day	3.08	3.10	0.03	0.48
DMC <sup>§</sup> , lb/lb	6.99	6.97	0.08	0.84

\*Zactran®, Merial Canada, Baie-D'Urfe, Quebec

\*\*Zuprevo™, Merck Animal Health, Intervet Canada Corp., Kirkland, Quebec

\*\*\*Sort weight = live body weight collected at approximately 30 days prior to slaughter

†DOF = days-on-feed from arrival to terminal weight sort

‡DDMI = daily dry matter intake, from arrival to terminal weight sort

‡ADG = average daily gain, from arrival to terminal weight sort

§DMC = dry matter conversion, from arrival to terminal weight sort

the most efficacious PMI for GAM or TIL in feedlot calves. Pharmacokinetics of GAM in plasma, pulmonary epithelial lining fluid, bronchoalveolar cells, and lung tissue in healthy cattle suggest a longer PMI of up to 15 days could be used.<sup>4</sup> Pharmacokinetics of tildipirosin in bovine plasma, lung tissue, and bronchial fluid in live, healthy cattle show a long T½ in lung and bronchial fluid, suggesting a PMI of 10 to 11 days could be used.<sup>7</sup>

The health crew was not completely blind to the treatment groups as products given to the cattle at processing was part of an individual animal's treatment history, which was available in the computer if an animal was pulled and treated. However, animals were not visually identified in any way that would identify the study group assignment. As a result, it is unlikely that there was any significant bias from the lack of blinding.

The unit of analysis in this study, the pen, could not be maintained as a unit from arrival until slaughter. The present study was discontinued at terminal weight sort due to mixing of cattle into different pens prior to sale to reduce carcass discounts. It is unlikely, however, that following the cattle another 30 days to slaughter would have significantly changed the comparative differences in health or performance, given that most BRD and arthritis occurred early in the feeding period.

Carcass data were not collected due to the feedlot's marketing system, therefore any economic differences in carcass merit could not be determined. Given there were no differences observed between the 2 treatment groups in health and performance from arrival to terminal weight sort, it is unlikely that there would have been significant differences in carcass weight, yield, or quality grades at slaughter.<sup>5</sup> Additional studies are warranted in different high-risk feedlot calves in order to determine the overall benefit of using GAM vs TIL metaphylactically at arrival processing.

The economic advantage of using GAM compared to TIL at arrival processing was \$4.13CAN/head. There were no significant differences in health or performance variables between treatment groups, therefore the economic difference was based simply on the difference in the cost of the metaphylaxis products. Changes in disease risk, PMI, and drug pricing will affect the net economic value of using GAM vs TIL as metaphylactic treatment for BRD in feedlot calves.

### Conclusion

There were no significant differences in morbidity or mortality due to BRD or arthritis, nor any growth differences between the 2 treatment groups. The net economic advantage of using gamithromycin instead of tildipirosin for metaphylactic treatment of winter-placed feedlot heifer calves was \$4.13CAN/head. This advantage was due simply to the current drug price differential of the 2 metaphylactic antimicrobials evaluated in the study.

### Endnotes

<sup>a</sup>DG Pro, ITS Global, Okotoks, AB

<sup>b</sup>M750 thermometer, GLA Agricultural Electronics, San Luis, Obispo, CA, USA

<sup>c</sup>Rumensin®, Elanco, Division Eli Lilly Canada Inc. & Elanco Canada Limited, Guelph, ON

<sup>d</sup>Tylan, Elanco, Division Eli Lilly Canada Inc. & Elanco Canada Limited, Guelph, ON

<sup>e</sup>Pyramid® 2 + Type II BVD, Boehringer Ingelheim (Canada) Ltd, Burlington, ON

<sup>f</sup>Vision® 8 Somnus with Spur®, Merck Animal Health, Intervet Canada Corp, Kirkland, QC

<sup>g</sup>Presponse® SQ, Boehringer Ingelheim (Canada) Ltd, Burlington, ON

<sup>h</sup>Bimectin™ Pour-On, Bimedia-MTC Animal Health Inc., Cambridge, ON

<sup>i</sup>Bimectin® Injection, Bimedia-MTC Animal Health Inc., Cambridge, ON

<sup>j</sup>SYNOVEX Choice®, Zoetis Canada Inc., Kirkland, QC

<sup>k</sup>Revalor 200®, Merck Animal Health, Intervet Canada Corp, Kirkland, QC

<sup>l</sup>Zactran®, Merial Canada, Baie-D'Urfé, QC

<sup>m</sup>Zuprevo™, Merck Animal Health, Intervet Canada Corp, Kirkland, QB

<sup>n</sup>Microsoft® Excel 2013, Redmond, WA, USA

<sup>o</sup>Stata 11, Stata Corp, College Station, TX, USA

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