# Field study of the comparative efficacy of gamithromycin and tulathromycin for the treatment of undifferentiated bovine respiratory disease complex in beef feedlot calves

Siddartha Torres, MVZ; Dan U. Thomson, DVM, PhD; Nora M. Bello, DVM, PhD; Bruce J. Nosky, DVM; Chris D. Reinhardt, PhD

**Objective**—To compare the efficacy of gamithromycin with that of tulathromycin for the treatment of undifferentiated bovine respiratory disease complex (BRDC) in feedlot calves.

**Animals**—1,049 weaned crossbred beef calves.

**Procedures**—At each of 6 feedlots, newly arrived calves with BRDC were administered a single dose of gamithromycin (6.0 mg/kg, SC; n = 523) or tulathromycin (2.5 mg/kg, SC; 526). Case-fatality and BRDC retreatment rates during the first 120 days after treatment, final body weight, and average daily gain (ADG), were compared between treatments. At 2 feedlots, calves were assigned clinical scores for 10 days after treatment to determine recovery rates for each treatment. Bioequivalence limits for gamithromycin and tulathromycin were calculated for outcomes for which there was no significant difference between treatments.

**Results**—Mean BRDC retreatment rate (17.7%) for calves administered gamithromycin was greater than that (9.0%) for calves administered tulathromycin. Mean case-fatality rate, final body weight, ADG, and clinical score 10 days after treatment did not differ significantly between treatments. Limits for mean differences within which gamithromycin was bioequivalent to tulathromycin were ± 2.4% for case-fatality rate, ± 13 kg for final body weight, and ± 0.1 kg/d for ADG.

**Conclusions and Clinical Relevance**—Calves administered gamithromycin had a higher BRDC retreatment rate than did calves administered tulathromycin; otherwise, the clinical efficacy did not differ between the 2 treatments for the treatment of BRDC in feedlot calves. (*Am J Vet Res* 2013;74:847–853)

The most common and costly disease of feedlot cattle in North America is BRDC,[1–3] which accounts for approximately 50% of the morbidity rate and 75% of deaths.[2] The US beef industry loses an estimated $1 billion annually because of treatment costs, reduced animal performance, and death from BRDC.[4–6] Bovine respiratory disease complex is a multifactorial syndrome caused by environmental factors, management practices, animal susceptibility, and viral and bacterial pathogens.[6] Results of multiple studies[7–12] indicate that a single dose of various injectable antimicrobials is beneficial for the treatment of BRDC in cattle. Tulathromycin, an antimicrobial belonging to the triamilide subclass of the macrolide antimicrobial group, has superior clinical efficacy, compared with the clinical efficacy of other antimicrobials, including tilmicosin, another macrolide, for the treatment of cattle with BRDC.[7,11,12] Gamithromycin is an azalide, another subclass of the macrolide antimicrobial group, that is labeled for the treatment of BRDC.[10,13] Both tulathromycin and gamithromycin inhibit bacterial protein synthesis by binding the 50S prokaryotic ribosomal subunit.[13] Macrolides are generally considered bacteriostatic; however, gamithromycin has bactericidal activity against *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni*, 3

**Abbreviations**

| | |
|---|---|
| ADG | Average daily gain |
| BRDC | Bovine respiratory disease complex |
| CI | Confidence interval |

Received July 11, 2012.
Accepted December 13, 2012.
From the Department of Clinical Sciences, College of Veterinary Medicine (Torres, Thomson), the Department of Statistics, College of Arts and Sciences (Bello), and the Department of Animal Sciences and Industry, College of Agriculture (Reinhardt), Kansas State University, Manhattan, KS 66506; and Large Animal Veterinary Services, Merial Ltd, 3239 Satellite Blvd, Duluth, GA 30096 (Nosky). Dr. Torres' present address is Merck Animal Health, 556 Morris Ave, Summit, NJ 07902.
Supported by Merial Ltd and the Beef Cattle Institute, Kansas State University.
This manuscript represents a portion of a dissertation submitted by Dr. Torres to the Department of Animal Sciences and Industry, College of Agriculture, Kansas State University as a partial fulfillment of the requirements for a Doctor of Philosophy degree.
Presented as an oral presentation at the Phi Zeta Research Day, College of Veterinary Medicine, Kansas State University, Manhattan, Kan, March 2012.
The authors thank Dr. Ron Tessman for technical assistance.
Address correspondence to Dr. Thomson (dthomson@vet.k-state.edu).

pathogens associated with BRDC.[13,14] To our knowledge, no field studies have been conducted to evaluate the health and performance outcomes for feedlot calves with BRDC that were treated with gamithromycin, compared with those for feedlot calves with BRDC that were treated with tulathromycin. The objectives of the study reported here were to compare the clinical efficacy of gamithromycin with that of tulathromycin for the treatment of BRDC in calves in a commercial feedlot setting and establish preliminary bioequivalence limits to assist veterinarians and feedlot producers in developing BRDC treatment protocols. We hypothesized that the clinical efficacy of gamithromycin would not differ from that of tulathromycin for the treatment of BRDC in feedlot calves because both antimicrobials belong to the macrolide group.

## Materials and Methods

**Animals**—Study procedures were approved by the Kansas State University Institutional Animal Care and Use Committee. The study was conducted at 6 commercial beef feedlots located in Colorado, Idaho, Kansas, Nebraska, Oklahoma, and Texas, the managers of which consented to participate in the study prior to its initiation. Weaned crossbred beef calves purchased from auction markets between October and December 2010 were considered for study enrollment. Calves were processed within 24 hours after arriving at the feedlot and placed in pens by arrival date. The health status of calves was monitored daily by feedlot personnel trained in cattle healthcare. Calves that had clinical signs of BRDC were moved to a centralized treatment area where they were weighed, examined, and assigned a clinical score on a scale of 0 to 4 (**Appendix**). Calves were enrolled in the study if they had a clinical score of 1 or 2 and a rectal temperature ≥ 40°C or a clinical score of 3, regardless of rectal temperature. Calves that were injured or debilitated or had a systemic disease (ie, gastrointestinal or musculoskeletal) other than BRDC were excluded from the study. The enrollment period was between December 10 and 12 for the Colorado feedlot, November 6 and 17 for the Idaho feedlot, October 25 and November 1 for the Kansas feedlot, October 26 and November 4 for the Nebraska feedlot, December 6 and 30 for the Oklahoma feedlot, and November 7 and 18 for the Texas feedlot. For the duration of the observation period (at least 120 days after treatment at each feedlot), calves were housed in open-air group pens, were fed a ration that was formulated to meet or exceed the National Research Council's requirements for maintenance and expected growth of beef cattle,[15] and had ad libitum access to water.

**Processing of calves**—Calves were processed within 24 hours after arrival at each respective feedlot. Processing included the application of an ear tag for individual calf identification, recording of body weight, surgical castration of sexually intact bull calves, and treatment for internal parasites with ivermectin[a] or doramectin[b] (Idaho feedlot). Additionally, calves were vaccinated against clostridial pathogens at the feedlots in Idaho,[c] Kansas,[d] Oklahoma,[e] and Texas.[f] Calves were administered a multivalent vaccine that contained antigens for bovine herpesvirus type 1, parainfluenza virus type 3, bovine respiratory syncytial virus, and bovine viral diarrhea virus types 1 and 2 at the feedlots in Colorado,[g] Idaho,[g] Kansas,[h] Nebraska,[i] and Oklahoma.[j] At the Texas feedlot, calves were administered a multivalent vaccine[k] that contained antigens for bovine herpesvirus type 1 and bovine viral diarrhea virus types 1 and 2. Also, calves were administered an anabolic implant that contained trenbolone acetate and estradiol at the feedlots in Idaho,[l] Kansas,[m] and Texas.[n] None of the calves were administered antimicrobials metaphylactically during processing.

**Study design**—Calves enrolled in the study were grouped in pairs on the basis of the order of processing through the handling facility to ensure that the number of calves in each treatment group was approximately equal at each feedlot. Within each pair, one calf was treated with a single dose of gamithromycin[o] (6.0 mg/kg [2 mL/50 kg], SC) and the other was treated with a single dose of tulathromycin[p] (2.5 mg/kg [1.25 mL/50 kg], SC) on the basis of a treatment randomization schedule that was created for each feedlot in a manner described.[16] The treatments were injected (maximum volume of antimicrobial, 10 mL/injection site) in the neck region cranial to the shoulder joint by a study investigator, and treatments were administered on the same side of the body for all calves within a given feedlot.

Following treatment, study calves at the Colorado and Oklahoma feedlots were housed in a single hospital pen where they were observed daily for 10 days and assigned a clinical score by feedlot personnel that were trained in cattle healthcare and who were unaware of the initial BRDC treatment administered to each calf. Study calves at the Idaho, Kansas, Nebraska, and Texas feedlots were returned to the pens from which they originated after treatment and monitored daily for the next 120 days (treatment [day 0] to day 120) by feedlot personnel who were trained in cattle healthcare and were unaware of the treatments that were administered to specific calves. At all 6 feedlots, calves with disorders (eg, gastrointestinal or musculoskeletal abnormalities) in addition to BRDC were treated similarly in accordance with standard treatment protocols regardless of the BRDC treatment (ie, gamithromycin or tulathromycin) administered. Health records for individual calves were maintained for the first 120 days after enrollment (treatment). Moribund calves were euthanized in accordance with the guidelines of the Animal Welfare Committee of the American Association of Bovine Practitioners.[17] Necropsies were performed by trained feedlot personnel on all calves that were euthanized or died between days 0 and 120. A diagnosis of BRDC was made on the basis of gross evidence of bronchopneumonia.

**Statistical analysis**—For each feedlot, calf health and performance data were obtained for the entire feeding period (ie, processing until removal from the feedlot for slaughter), although the length of the feeding period varied from 120 to 180 days among the feedlots. For each calf, initial body weight was defined as the individual body weight of the calf at enrollment (ie, treatment with gamithromycin or tulathromycin [day

0]) and final body weight was defined as the individual body weight of the calf immediately prior to transport for slaughter after approximately 120 (Colorado, Idaho, Nebraska, and Oklahoma), 170 (Texas), or 180 (Kansas) days on feed. For each calf, ADG was calculated as the final body weight minus the initial body weight divided by the number of days that calf was on feed.

The BRDC retreatment rate for each treatment group was calculated as the number of calves in that treatment group that were treated for BRDC a second time within the first 120 days after enrollment divided by the number of calves in that treatment group. Calves that died or were euthanized for reasons other than BRDC were excluded from the case-fatality rate calculation. The case-fatality rate for each treatment group was defined as the number of calves in that treatment group that died because of BRDC divided by the number of calves in that treatment group.

Continuous outcome variables (initial and final body weights, rectal temperature at enrollment, and ADG) were evaluated via general linear mixed models. Models for the outcomes initial body weight and rectal temperature at enrollment included treatment (gamithromycin or tulathromycin) as a fixed effect and enrollment date and feedlot (Colorado, Idaho, Kansas, Nebraska, Oklahoma, or Texas) as random effects. The interaction between treatment and feedlot (proxy for the experimental unit [ie, calves clustered within treatment groups within feedlots]) was assessed as a random effect and subsequently removed from each model because the variance component converged to 0. Models for the outcomes final body weight and ADG included treatment as a fixed effect and feedlot and the interaction between feedlot and treatment as random effects. Additionally, initial body weight and number of days on feed were assessed as fixed effects in the models for final body weight and ADG; however, the final model for ADG did not include number of days on feed because of a lack of significance ($P > 0.05$).

Categorical outcome variables (BRDC retreatment and case-fatality rates) were evaluated via generalized linear mixed models with a logit link function. Each model included treatment as a fixed effect and feedlot as a random effect. The interaction between treatment and feedlot was assessed but excluded from the final model for each outcome because the variance component converged to 0. Additionally, rectal temperature at enrollment and initial body weight were assessed as fixed effects in each model; however, the final model for case-fatality rate did not include rectal temperature because of a lack of significance.

The clinical scores obtained daily for 10 days after treatment for the study calves at the feedlots in Colorado and Oklahoma were assumed to have a categorical multinomial distribution and were evaluated via a generalized linear mixed model with a cumulative logit link function. Fixed effects included in the model were treatment, observation day (ie, 0 [day of treatment] to 10 days after treatment), and the interaction between treatment and observation day. Random effects included in the model were the interaction between feedlot and arrival date, which represented a blocking factor for treatment, and calf nested within treatment for each feedlot and arrival date combination, which accounted for the experimental unit for treatment and the repeated measures for each calf.

The outcomes for calves treated with gamithromycin were compared with those for calves treated with tulathromycin by use of classical hypothesis testing and the calculation of the ANOVA type III *F* test statistics; a mean treatment difference with $P \leq 0.05$ was considered significant. For each outcome variable for which no significant difference was detected between the 2 treatment groups via classical hypothesis testing, bioequivalence limits were calculated as described.[16] Statistical software[q] was used to perform all analyses. Methods used to estimate degrees of freedom, adjust the estimation of SEMs, and perform pairwise comparisons were as described.[16]

## Results

**Animals—**A total of 1,049 calves with BRDC were enrolled in the study, including 100 calves at the Colorado feedlot (mean ± SD initial body weight, 220 ± 22 kg), 200 at the Idaho feedlot (244 ± 25 kg), 216 at the Kansas feedlot (227 ± 21 kg), 196 at the Nebraska feedlot (244 ± 28 kg), 112 at the Oklahoma feedlot (236 ± 21 kg), and 225 at the Texas feedlot (244 ± 18 kg). All study calves arrived at the feedlot within a period of 1 (Colorado and Kansas), 6 (Nebraska), 8 (Idaho and Oklahoma), or 10 (Texas) days. Five hundred twenty-three calves were treated with gamithromycin, and 526 calves were treated with tulathromycin. No adverse reactions were observed in any of the calves following treatment administration, and none of the calves were removed from the study for reasons other than death prior to day 120. Mean initial body weight ($P = 0.41$), rectal temperature ($P = 0.79$), proportion of calves with a fever (≥ 40°C), and number of days on feed at enrollment ($P = 0.52$; **Table 1**) and the proportion of bull calves that were castrated during processing ($P = 0.61$) did not differ significantly between the treatment groups, which suggested that the randomization procedure used was successful.

**BRDC retreatment rate—**During the 120 days after the initial BRDC treatment, 125 calves in the gamithromycin treatment group and 71 calves in the tulathromycin treatment group were retreated for BRDC at least once (**Table 2**). The majority (191/196 [97%]) of calves were retreated for BRDC within 35 days after initial treatment. The mean ± SEM BRDC retreatment rate for all calves was 12.8 ± 5%; however, the mean ± SEM BRDC retreatment rate for calves treated with gamithromycin (17.7 ± 6.7%) was significantly ($P < 0.01$) greater, compared with that for calves treated with tulathromycin (9.0 ± 3.9%).

Initial body weight and rectal temperature at enrollment were significantly associated with BRDC retreatment rate. When the initial body weight was fixed at 233 kg (the mean initial body weight for all study calves) and treatment group was controlled, the odds that a calf would require retreatment for BRDC was 1.55 (95% CI, 1.01 to 2.39) for every 50-kg decrease in initial body weight. Thus, the risk of a calf requiring retreatment for BRDC during the first 120 days after

Table 1—Mean ± SEM initial body weight, rectal temperature, proportion of calves with a fever (rectal temperature, ≥ 40°C), and number of days on feed at enrollment for weaned crossbred beef calves with BRDC that were treated with a single dose of gamithromycin (6.0 mg/kg [2 mL/50 kg], SC; n = 523) or tulathromycin (2.5 mg/kg [1.25 mL/50 kg], SC; 526).

| Variable | Treatment group: Gamithromycin | Treatment group: Tulathromycin | *P* value |
|---|---|---|---|
| Initial body weight (kg) | 235 ± 1.6 | 236 ± 1.6 | 0.41 |
| Rectal temperature (°C) | 40.2 ± 0.1 | 40.2 ± 0.1 | 0.79 |
| Proportion of calves with fever (%) | 64.5 ± 5.0 | 60.4 ± 6.0 | 0.11 |
| Days on feed (d) | 3.6 ± 0.7 | 3.7 ± 0.7 | 0.52 |

The study was conducted at 6 commercial beef feedlots located in Colorado, Idaho, Kansas, Nebraska, Oklahoma, and Texas. Calves were purchased from auction markets between October and December 2010 and were enrolled in the study if they had clinical signs of BRDC and were assigned a clinical score of 1 or 2 and a rectal temperature ≥ 40°C or a clinical score of 3, regardless of rectal temperature. Calves that were injured or debilitated or had a systemic disease (ie, gastrointestinal or musculoskeletal) other than BRDC were excluded from the study.

Table 2—Number of calves from Table 1 that were retreated (second treatment) for BRDC and the cumulative BRDC retreatment rate by days after treatment.

| Days after treatment | Treatment group: Gamithromycin | Treatment group: Tulathromycin | Total | Cumulative BRDC retreatment rate |
|---|---|---|---|---|
| 7 | 5 | 5 | **10** | 5 |
| 14 | 51 | 35 | **86** | 49 |
| 21 | 43 | 12 | **55** | 77 |
| 28 | 12 | 14 | **26** | 90 |
| 35 | 9 | 5 | **14** | 97 |
| 42 | 1 | 0 | **1** | 98 |
| 49 | 2 | 0 | **2** | 99 |
| 63 | 1 | 0 | **1** | 99 |
| 84 | 1 | 0 | **1** | 100 |
| **Total** | **125** | **71** | **196** | **NA** |

NA = Not applicable.
*See* Table 1 for remainder of key.

Table 3—Number of calves from Table 1 that died because of BRDC and the cumulative case-fatality rate by days after treatment.

| Days after treatment | Treatment group: Gamithromycin | Treatment group: Tulathromycin | Total | Cumulative case-fatality rate (%) |
|---|---|---|---|---|
| 7 | 8 | 16 | **24** | 29 |
| 14 | 7 | 10 | **17** | 49 |
| 21 | 1 | 1 | **2** | 52 |
| 28 | 8 | 4 | **12** | 66 |
| 35 | 8 | 2 | **10** | 78 |
| 42 | 3 | 1 | **4** | 83 |
| 49 | 3 | 1 | **4** | 88 |
| 56 | 0 | 1 | **1** | 89 |
| 70 | 1 | 0 | **1** | 90 |
| 77 | 2 | 1 | **3** | 94 |
| 84 | 0 | 1 | **1** | 95 |
| 91 | 1 | 0 | **1** | 96 |
| 98 | 0 | 1 | **1** | 98 |
| 105 | 2 | 0 | **2** | 100 |
| **Total** | **44** | **39** | **83** | **NA** |

*See* Tables 1 and 2 for key.

Table 4—Mean ± SEM and bioequivalence limits for case-fatality rate during the first 120 days after treatment, final body weight, and ADG for the calves of Table 1.

| Variable | Treatment group: Gamithromycin | Treatment group: Tulathromycin | Bioequivalence limits |
|---|---|---|---|
| Case-fatality rate (%) | 2.4 ± 4.2 | 3.7 ± 4.2 | ± 2.4 |
| Final body weight (kg) | 450 ± 7.0 | 456 ± 7.0 | ± 13.0 |
| ADG (kg/d) | 1.52 ± 0.06 | 1.57 ± 0.06 | ± 0.1 |

For each calf, ADG was calculated as the final body weight minus the initial body weight divided by the number of days that calf was on feed. The treatment effect of gamithromycin was compared with that of tulathromycin via a generalized linear mixed model with a logit link function for case-fatality rate and via general linear mixed models for final body weight and ADG. The treatment effects did not differ significantly ($P > 0.05$) for any of the outcomes. The bioequivalence limits were determined by the assumption of a 5% type I error rate, defined by the 90% CI for the mean difference between the 2 treatment groups, and expressed in the same units as the treatment mean.

treatment was negatively associated with initial body weight; the less a calf weighed at enrollment, the greater its risk of requiring retreatment for BRDC. When rectal temperature at enrollment was fixed at 39.9°C, the odds that a calf would require retreatment for BRDC was 1.8 (95% CI, 1.4 to 2.3) for every 1°C increase in rectal temperature at enrollment. Hence, the risk of a calf requiring retreatment for BRDC during the first 120 days after treatment was positively associated with rectal temperature at enrollment; the higher a calf's rectal temperature was above 39.9°C, the greater its risk of requiring retreatment.

**BRDC case-fatality rate—**During the first 120 days after the initial BRDC treatment, 44 calves in the gamithromycin treatment group and 39 calves in the tulathromycin treatment group died because of BRDC (**Table 3**). The majority (65/83 [78%]) of calves died within 35 days after the initial BRDC treatment. The mean ± SEM case-fatality rate for all calves was 4.2 ± 2%. The case-fatality rate for calves in the gamithromycin treatment group did not differ significantly from that for calves in the tulathromycin treatment group, and the bioequivalence limits for case-fatality rate were ± 2.4% (**Table 4**).

Rectal temperature at enrollment was positively associated with the BRDC case-fatality rate in a manner similar to that for BRDC retreatment rate. When rectal temperature at enrollment was fixed at 39.9°C, the odds that a calf would die because of BRDC during the first 120 days after initial BRDC treatment were 1.94 (95% CI, 1.51 to 2.48) for each 1°C increase in rectal temperature at enrollment.

**Animal performance—**Final body weight and ADG did not differ significantly between the 2 treatment groups. The mean ± SEM for each treatment group for final body weight and ADG and the corresponding bioequivalence limits were summarized (Table 4).

**Clinical score analysis—**Clinical scores during the 10 days after initial BRDC treatment were evaluated for calves at the Colorado and Oklahoma feedlots only. No significant ($P = 0.97$) difference was detected between the clinical scores for the calves treated with gamithromycin and the clinical scores for the calves treated with tulathromycin. Additionally, the clinical scores de-

creased significantly ($P < 0.01$) over time, regardless of the treatment.

## Discussion

Results of the present study indicated that the clinical efficacy of the labeled dose of gamithromycin did not differ significantly from that of the labeled dose of tulathromycin for the treatment of BRDC in beef feedlot calves for all outcomes evaluated except BRDC retreatment rate. Calves with BRDC that were treated with gamithromycin had a higher BRDC retreatment rate than did calves with BRDC that were treated with tulathromycin. Results of other studies[7–12] indicate that both gamithromycin and tulathromycin are clinically efficacious for the treatment of BRDC; however, to our knowledge, the present study was the first to compare the clinical efficacy of gamithromycin with that of tulathromycin for the treatment of BRDC in feedlot cattle.

The calves enrolled in the present study were considered to be at high risk of developing BRDC because they had a low body weight (mean ± SEM, 233.8 ± 24 kg) at feedlot arrival, were acquired from auction markets where they were commingled with cattle from multiple sources and likely exposed to many bovine pathogens, and were stressed from transportation, and because of the time of year during which they were introduced to the feedlot. Data regarding the geographic location of the auction markets from which the study calves were obtained was unavailable; therefore, we were unable to estimate or compare the length of time or distance that calves in each treatment group were transported. The incidence of BRDC in feedlot cattle generally increases in the fall and early winter because of sudden extreme changes in temperature and weather.[18,19]

We chose to monitor health outcomes for a minimum of 120 days after calves were initially treated for BRDC in the present study because we wanted to assess the long-term efficacy of gamithromycin and tulathromycin for the treatment of BRDC. Other studies[7–11] that were conducted to evaluate the efficacy of various antimicrobials for the treatment of BRDC only monitored health outcomes for 10 to 28 days after treatment. Interestingly, in the present study, no calves were retreated for or died because of BRDC greater than 105 days after initial treatment, and at 35 days after the initial treatment, 97% of the cumulative retreatment rate and 78% of the cumulative case-fatality rate had been observed. Therefore, we suggest that an observation period of 35 days is sufficient to evaluate the clinical efficacy of antimicrobials for the treatment of BRDC in feedlot cattle.

In the present study, the BRDC retreatment rate for calves that were treated with gamithromycin was higher than that for calves that were treated with tulathromycin. Although initial body weight and rectal temperature at enrollment were negatively and positively associated with BRDC retreatment rate, respectively, the interaction between initial body weight and treatment and between fever (rectal temperature, ≥ 40°C) and treatment were not significantly associated with BRDC retreatment rate. Therefore, the effect of treatment did not vary among values observed for initial body weight and rectal temperature at enrollment.

The reason calves treated with gamithromycin had a higher BRDC treatment rate than did calves treated with tulathromycin in the present study is unknown. Gamithromycin and tulathromycin are both macrolides and have the same mechanism of action against microbes; therefore, we did not expect the clinical efficacy of the 2 drugs to differ for any of the outcomes evaluated. However, these results are similar those of other studies,[7,11] in which the efficacy of tulathromycin was compared with that of tilmicosin, another macrolide. In 1 study,[11] the BRDC cure rate for calves treated with tulathromycin was significantly higher than that for calves treated with tilmicosin at 1 of 2 feedlots; however, statistical analysis to compare the BRDC cure rates across both feedlots was not performed. In the other study,[7] the BRDC cure rate for calves treated with tulathromycin was significantly higher than that for calves treated with tilmicosin across 4 feedlots as well as within each feedlot.

A possible reason for the significant difference in the BRDC retreatment rates for calves treated with gamithromycin and those treated with tulathromycin in the present study is that a disproportionate number of calves were misclassified as having BRDC between the 2 treatment groups. Clinical diagnosis of BRDC in cattle is generally made on the basis of a combination of subjective and objective observations,[19] and use of such a method for diagnosis of BRDC has a low sensitivity (61.8%) and specificity (62.8%).[20] Consequently, a substantial proportion of cattle with BRDC are misclassified as clinically normal and a substantial proportion of clinically normal cattle are misclassified as having BRDC. In 1 study,[21] only 55.4% (211/380) of cattle that had been treated once for BRDC had lung lesions observed at slaughter, whereas in another study,[22] 78% (128/164) of cattle that had been treated for BRDC had lung lesions observed at slaughter. The development of a more sensitive and specific method for diagnosing BRDC in cattle will allow for a more accurate assessment of BRDC morbidity and retreatment rates in studies involving feedlot cattle.

The BRDC case-fatality rate for all calves in the present study was 4.2% and did not differ significantly between calves treated with gamithromycin and tulathromycin. The BRDC case-fatality rate for the calves of the present study was higher than that for calves in another study,[7] in which the clinical efficacy of tulathromycin was compared with that of tilmicosin for the treatment of BRDC in feedlot calves; nevertheless, the results were similar in that there was no significant difference in the case-fatality rates between calves treated with tulathromycin and calves treated another macrolide (tilmicosin). In another study,[11] in which the clinical efficacy of tulathromycin was compared with that of tilmicosin for the treatment of BRDC in calves at 2 feedlots, the BRDC case-fatality rate for calves treated with tilmicosin was significantly higher than that for calves treated with tulathromycin at 1 feedlot, but the BRDC case-fatality rates for calves treated with tulathromycin and those treated with tilmicosin did not differ significantly at the other feedlot.

The mean ADG for calves during the first 120 days after initial treatment for BRDC did not differ between

calves treated with gamithromycin and calves treated with tulathromycin in the present study. In another study,[11] the mean ADG for calves treated with tulathromycin was significantly greater than that for calves treated with tilmicosin during the first 28 days after treatment; however, the mean ADG did not differ between calves treated with tulathromycin and calves treated with tilmicosin during the entire feeding period (ie, time from treatment until slaughter). Results of 1 study[1] indicate that feedlot cattle that are treated for BRDC and survive have a compensatory weight gain 135 to 238 days after treatment, which suggests that evaluation of ADG as a measure of an antimicrobial's efficacy for the treatment of BRDC is clinically relevant only when it is measured during short periods immediately after treatment. Additional studies, in which ADG is serially evaluated for short periods at various times after BRDC treatment, are necessary to better evaluate compensatory weight gain in cattle that survive BRDC.

In the statistical analyses performed for the present study, feedlot and the interaction between feedlot and treatment were modeled as random effects to account for interfeedlot variability.[23] This allowed us to make broad inferences for all 6 feedlots and the greater US feedlot population in general, assuming that the 6 feedlots of this study were a representative sample of US feedlots.[23] These models could not be used to make inferences within each feedlot, and separate statistical analyses for each feedlot were not performed.

The bioequivalence limits for gamithromycin and tulathromycin calculated for case-fatality rate and final body weight in the present study were much narrower than those calculated for case-fatality rate and final body weight in another study[16] conducted by our laboratory group. In that study,[16] the clinical efficacy of gamithromycin was compared with that of tulathromycin for the control (ie, metaphylaxis) of BRDC in feedlot cattle, whereas in the present study, the clinical efficacy of gamithromycin was compared with that of tulathromycin for the treatment of cattle with BRDC. Therefore, the calves that were administered gamithromycin and tulathromycin in the other study[16] were clinically normal, whereas those in the present study had clinical signs of BRDC. The width of the bioequivalence limits is a function of the variability within the data. Because calves had to have clinical signs of BRDC to be enrolled in the present study, it is likely that this study population was more homogeneous than the population of calves enrolled in the other study,[16] which might explain why the bioequivalence limits for case-fatality rate and final body weight in the present study were narrower than those in the other study. Regardless, as discussed in the other study,[16] the calculation of bioequivalence limits for 2 similar drugs is a rather novel approach for the evaluation of data obtained from field studies and provides information that cannot be obtained via classical hypothesis testing. This information can be beneficial for veterinarians and livestock producers who routinely have to choose between 2 competing products for the treatment of a large number of animals on the basis of efficacy as well as cost.

In the present study, the clinical efficacy of the labeled dose of gamithromycin did not differ from that of the labeled dose of tulathromycin for the treatment of BRDC in feedlot calves for all outcomes evaluated except BRDC retreatment rate. The BRDC retreatment rate for calves that were treated with gamithromycin was significantly higher than that for calves that were treated with tulathromycin. The bioequivalence limits for gamithromycin and tulathromycin calculated for case-fatality rate, final body weight, and ADG should be considered preliminary, but they provide additional information that could be useful for veterinarians and feedlot producers when making decisions regarding treatment of BRDC in a large population of cattle.

a. Ivomec Plus, Merial Ltd, Duluth, Ga.
b. Dectomax, Pfizer Animal Health, New York, NY.
c. Vision 8, Intervet/Schering-Plough Animal Health, Millsboro, Del.
d. Caliber 7, Boehringer Ingelheim Vetmedica Inc, St Joseph, Mo.
e. Vision 7, Intervet/Schering-Plough Animal Health, Millsboro, Del.
f. Essential 2, Colorado Serum Co, Denver, Colo.
g. Pyramid 5, Boehringer Ingelheim Vetmedica Inc, St Joseph, Mo.
h. Bovishield Gold 5, Pfizer Animal Health, New York, NY.
i. Express 5, Boehringer Ingelheim Vetmedica Inc, St Joseph, Mo.
j. Titanium 5, Agri Laboratories Ltd, St Joseph, Mo.
k. Vista 3 SC, Intervet/Schering-Plough Animal Health, Millsboro, Del.
l. Revalor G, Intervet/Schering-Plough Animal Health, Millsboro, Del.
m. Component TE- IH, Eli Lilly and Co, Indianapolis, Ind.
n. Revalor-IH, Intervet/Schering-Plough Animal Health, Millsboro, Del.
o. Zactran, Merial Ltd, Duluth, Ga.
p. Draxxin, Pfizer Animal Health, New York, NY.
q. PROC GLIMMIX, SAS, version 9.3, SAS Institute Inc, Cary, NC.

## References


1. Snowder GD, Van Vleck LD, Cundiff LV, et al. Bovine respiratory disease in feedlot cattle: environmental, genetic, and economic factors. *J Anim Sci* 2006;84:1999–2008.
2. Babcock AH, White BJ, Dritz SS, et al. Feedlot health and performance effects associated with the timing of respiratory disease treatment. *J Anim Sci* 2009;87:314–327.
3. Schneider MJ, Tait RG, Busby WD, et al. An evaluation of bovine respiratory disease complex in feedlot cattle: impact on performance and carcass traits using treatment records and lung lesion scores. *J Anim Sci* 2009;87:1821–1827.
4. Garcia MD, Thallman RM, Wheeler TL, et al. Effect of bovine respiratory disease and overall pathogenic disease incidence on carcass traits. *J Anim Sci* 2010;88:491–496.
5. McVey DS. BRD research needs in the next 10–20 years. *Anim Health Res Rev* 2009;10:165–167.
6. Nickell JS, White BJ. Metaphylactic antimicrobial therapy for bovine respiratory disease in stocker and feedlot cattle. *Vet Clin North Am Food Anim Pract* 2010;26:285–301.
7. Kilgore WR, Spensley MS, Sun F, et al. Therapeutic efficacy of tulathromycin, a novel triamilide antimicrobial, against bovine respiratory disease in feeder calves. *Vet Ther* 2005;6:143–153.
8. Nutsch RG, Skogerboe TL, Rooney KA, et al. Comparative efficacy of tulathromycin, tilmicosin, and florfenicol in the treatment of bovine respiratory disease in stocker cattle. *Vet Ther* 2005;6:167–179.
9. Schunicht OC, Booker CW, Guichon PT, et al. An evaluation of the relative efficacy of tulathromycin for the treatment of undifferentiated fever in feedlot calves in Nebraska. *Can Vet J* 2007;48:600–606.
10. Sifferman RL, Wolff WA, Holste JE, et al. Field efficacy evaluation of gamithromycin for treatment of bovine respiratory disease in cattle at feedlots. *J Appl Res Vet Med* 2011;9:166–175.

11. Skogerboe TL, Rooney KA, Nutsch RG, et al. Comparative efficacy of tulathromycin versus florfenicol and tilmicosin against undifferentiated bovine respiratory disease in feedlot cattle. *Vet Ther* 2005;6:180–196.
12. Wellman NG, O'Connor AM. Meta-analysis of treatment of cattle with bovine respiratory disease with tulathromycin. *J Vet Pharmacol Ther* 2007;30:234–241.
13. Giguère S, Huang R, Malinski TJ, et al. Disposition of gamithromycin in plasma, pulmonary epithelial lining fluid, bronchoalveolar cells, and lung tissue in cattle. *Am J Vet Res* 2011;72:326–330.
14. Forbes AB, Ramage C, Sales J, et al. Determination of the duration of antibacterial efficacy following administration of gamithromycin using a bovine *Mannheimia haemolytica* challenge model. *Antimicrob Agents Chemother* 2011;55:831–835.
15. National Research Council. Tables of nutrient requirements. In: *Nutrient requirements of beef cattle*. 7th ed. Washington, DC: National Academies Press, 1996;102–112.
16. Torres S, Thomson DU, Bello NM, et al. Field study of the comparative efficacy of gamithromycin and tulathromycin for the control of undifferentiated bovine respiratory disease complex in beef feedlot calves at high risk of developing respiratory tract disease. *Am J Vet Res* 2013;74:839–846.
17. American Association of Bovine Practitioners Animal Welfare Committee. *Practical euthanasia of cattle: considerations for the producer, livestock market operator, livestock transporter, and veterinarian*. Auburn, Ala: American Association of Bovine Practitioners, 1999.
18. Taylor JD, Fulton RW, Lehenbauer TW, et al. The epidemiology of bovine respiratory disease: what is the evidence for predisposing factors? *Can Vet J* 2010;51:1095–1102.
19. Loneragan GH, Dargatz DA, Morley PS, et al. Trends in mortality ratios among cattle in US feedlots. *J Am Vet Med Assoc* 2001;219:1122–1127.
20. White BJ, Renter DG. Bayesian estimation of the performance of using clinical observations and harvest lung lesions for diagnosing bovine respiratory disease in post-weaned beef calves. *J Vet Diagn Invest* 2009;21:446–453.
21. Thompson PN, Stone A, Schultheiss WA. Use of treatment records and lung lesion scoring to estimate the effect of respiratory disease on growth during early and late finishing periods in South African feedlot cattle. *J Anim Sci* 2006;84:488–498.
22. Wittum TE, Woollen NE, Perino LJ, et al. Relationships among treatment for respiratory tract disease, pulmonary lesions evident at slaughter and rate of weight gain in feedlot cattle. *J Am Vet Med Assoc* 1996;209:814–818.
23. Tempelman RJ. Invited review: assessing experimental designs for research conducted on commercial dairies. *J Dairy Sci* 2009;92:1–15.

## Appendix

Scale used to assign clinical scores to weaned crossbred beef calves with BRDC that were treated with a single dose of gamithromycin (6.0 mg/kg [2 mL/50 kg], SC; n = 523) or tulathromycin (2.5 mg/kg [1.25 mL/50 kg], SC; 526) at 6 commercial feedlots located in Colorado, Idaho, Kansas, Nebraska, Oklahoma, and Texas.

| Score | Description |
|---|---|
| 0 | Clinically normal; nothing unusual about the animal's attitude and no abnormal respiratory signs present |
| 1 | Mild signs of depression (animal somewhat slow coming to feed bunk but did eat); mild respiratory signs present (serous nasal or ocular discharge or cough) |
| 2 | Moderate signs of depression (animal's head or ears drooping slightly, reluctant to move about, or reluctant to come to the feed bunk); moderate respiratory distress (mucosus or mucopurulent nasal or ocular discharge or increase in respiratory rate or effort) |
| 3 | Severe signs of depression (animal has a pronounced head or ear droop or is very reluctant to move); severe respiratory distress (marked increase in respiratory rate or effort, including open-mouth breathing, abdominal breathing, or extended neck) |
| 4 | Moribund |