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Comparison of gamithromycin post-treatment intervals for beef cattle naturally affected with bovine respiratory disease

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Abstract

The primary objective of this study was to compare different gamithromycin post-treatment intervals (PTI) on clinical health outcomes in cattle naturally affected with bovine respiratory disease (BRD). Eight hundred cattle identified with BRD by pen riders, rectal temperature ≥ 104.0°F (≥ 40°C), and no previous treatments were randomized in a 1:1:1:1 ratio to 3-, 6-, 9-, or 12-day PTI within each lot. Cattle treated for BRD were returned to their home pen, and followed for 60 days (d) to monitor subsequent health outcomes. Cattle were categorized by type (dairy-beef or native). General and generalized linear mixed models were used for statistical analyses. First treatment success (P = 0.012) and BRD case fatality risk (P = 0.032) were different among PTI groups. The 9-d PTI group had the greatest first treatment success, which was different (P = 0.008) than the 3-d PTI. The 12-d PTI group had the poorest BRD case fatality risk, which was different (P = 0.071) than the 9-d PTI group. There were no significant differences between the 6- and the 9-d PTI groups. Dairy-beef cattle had an approximately 2-fold higher BRD case fatality risk (P = 0.012) than natives. Results will help practitioners to optimally use gamithromycin in the field.

Key words: BRD, dairy-beef cross, feedlot, PTI, treatment, gamithromycin

Introduction

Gamithromycin[a] is a 15-membered semi-synthetic ring azalide macrolide, with a unique alkylated nitrogen at the 7a carbon of the lactone ring, commercially available for treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis* in beef and non-lactating dairy cattle.[6,25] Macrolides are generally considered bacteriostatic;[12] however, gamithromycin has bactericidal effects against *Mannheimia haemolytica*.[8,11] Previous field efficacy studies have demonstrated gamithromycin to be an effective antimicrobial for treatment of BRD.[6,13,16] Therapeutic concentrations of gamithromycin were present in pulmonary epithelial lining fluid, bronchoalveolar lavage cells, and lung tissue cells within 30 min and persisted for 7 d in pulmonary epithelial lining fluid or greater than 15 d in bronchoalveolar lavage cells and lung tissue cells after a single administration in healthy cattle.[10] However, pharmacokinetics in cattle with BRD have been shown to be different than in clinically healthy cattle.[7] Pharmacokinetics and pharmacodynamic data may not provide optimal information for recommended post-treatment interval (PTI).[3] The PTI is the amount of time required to pass before the animal is eligible for additional therapy. In the multiple comparison studies performed on treatment for BRD, few studies have evaluated varying PTIs. A previous publication evaluated different PTIs of tilmicosin.[b,5] Data are available in technical bulletins where PTIs for tulathromycin[c,20] and ceftiofur crystalline free acid[d,21,22] were compared. All 3 trials showed that extending the PTI to 7 d resulted in improved health outcomes; however, there are limited published data available for optimal PTI for gamithromycin.

Beef sires are used on dairy cows to create dairy-beef cattle to be marketed through the feedlot;[19,24] however, published literature evaluating products and management strategies in dairy-beef cross feedlot cattle is limited. The primary objective of this study was to compare different gamithromycin post-treatment intervals on clinical health outcomes in cattle naturally affected with BRD. Our hypothesis was that extending the PTI would improve treatment outcomes. The secondary objective was to evaluate health outcomes in dairy-beef cross cattle compared to native beef cattle.

Materials and Methods

The study was performed at Hy-Plains Feedyard, LLC located near Montezuma, Kansas, which is a custom cattle-feeding operation. The study began December 15, 2019 and concluded June 19, 2020. All procedures were approved by the Boehringer Ingelheim Animal Health USA, Inc Animal Care and Use Committee (APS-19-221) prior to the study initiating.

Sample Size

First-treatment success was considered the primary outcome for the study and used for sample size estimates. Sample size was based on ability to detect a difference of 12.5% with a baseline of 80% first-treatment success. Alpha was set at 0.05, and beta set to 0.20 using a commercial software package,[e] resulting in 193 cattle per PTI treatment group.

Animals

Cattle throughout the feedyard were observed daily by pen riders for identification of BRD. Identification of BRD was made based upon visual evaluation of physical appearance, attitude, gauntness, nasal discharge, and/or reluctance to move. All pen riders had a minimum of 5 years of experience riding pens in a commercial feedlot, and pen riders would rotate sections of the feedyard they would ride throughout the week. Any calf which displayed clinical signs was moved from the home pen to the hospital for confirmatory diagnosis and either enrollment into or exclusion from the study. The feedlot had an average population of 32,109 head during the enrollment period.

Inclusion Criteria

All cattle identified by pen riders with clinical signs of BRD were evaluated by a veterinarian (MET) prior to enrollment. Cattle were assigned a subjective clinical attitude score (Table 1) by the veterinarian prior to enrollment. Inclusion criteria for the study were identified morbid with BRD by pen rider, no previous treatments for disease, rectal temperature ≥ 104.0°F (≥ 40°C), clinical attitude score 1 to 3, estimated > 60 days to harvest, and absence of clinical signs of disease in other organ systems.

Table 1. Description of clinical attitude scoring system used to assess cattle upon enrollment in a study comparing various post-treatment intervals following treatment of BRD with gamithromycin.

Clinical attitude score	Criteria
0	Normal; bright; alert; responsive
1	Mild depression; signs of weakness usually not present
2	Moderate depression; some signs of weakness; may be reluctant to stand
3	Severe depression; difficulty standing; head lowered or extended
4	Moribund; unable to stand

All lots in the commercial feedlot which did not receive a metaphylactic antimicrobial during arrival processing were eligible to be enrolled beginning at 1 day on feed (DOF). Lots which received a metaphylactic antimicrobial of tilmicosin[b] (6 mg/lb [13.2 mg/kg] of body weight [BW] subcutaneously [SC]; 2.0 mL/100 lb [45.5 kg] of BW) or tulathromycin[c] (1.13 mg/lb [2.5 mg/kg] BW; 1.1 mL/100 lb of BW SC) were eligible for inclusion beginning at 21 DOF. Cattle pulled for BRD from lots which were metaphylactically administered an antimicrobial and pulled for BRD prior to 21 DOF were excluded from the study and treated according to feedlot operating procedures. The decision to metaphylactically treat individual lots during arrival processing was made by feedlot personnel based upon subjective risk classification. Risk classification was based upon origin, transportation distance, shrink, and visual appearance of the cattle upon arrival to the feedlot.

Enrollment

Upon meeting the inclusion criteria, cattle were randomized in a 1:1:1:1 ratio to 1 of 4 PTI groups within each eligible lot: 3-d PTI, 6-d PTI, 9-d PTI, or 12-d PTI following treatment with gamithromycin (2.72 mg/lb [6 mg/kg] BW; 2.0 mL/110 lb of BW SC). Table 2 provides an overview for the timing of events which occurred for each calf. Enrollment was performed by different personnel (MET) than pen riders to maintain blinding of treatment groups.

An enrollment form was created to assign cattle to PTI treatment group in groups of 4 within each lot. A random number generator[f] was used to create random numbers for each blank on the enrollment form. The 4 PTI treatment groups were written on a piece of paper and drawn from a hat to determine treatment group assignment based upon random number generated within each group of 4. The 3-d PTI was assigned to smallest random number within the group, 12-d PTI assigned to the second-smallest random

Table 2. Outline of study timeline events for each individual calf enrolled in a comparative study of post-treatment intervals (PTI) following treatment of BRD with gamithromycin.

Study day	Events
0	Enrollment
1	
2	
3	3-day PTI eligible for retreatment
4	
5	
6	6-day PTI eligible for retreatment
7	
8	
9	9-day PTI eligible for retreatment
10	
11	
12	12-day PTI eligible for retreatment
60	Study conclusion

number within the group, 9-d PTI to the third-smallest random number within the group, and 6-d PTI to the greatest random number within the group. The first calf which met the inclusion criteria was assigned to PTI group assigned to the first blank on the enrollment form. The next calf from the same lot which met the inclusion criteria was assigned to the second blank on the enrollment form, and each calf from a different lot was assigned to a different group of 4. An individual lot could be enrolled to more than 1 group of 4 if there were more than 4 calves enrolled into the study from the same lot. Cattle were randomized in an effort to evenly distribute treatments within lot.

Duplicate ear tags were used to identify each calf upon study enrollment. The date a calf was eligible for retreatment was written on the tag for the pen rider to be able to identify when eligible for additional treatment. No information about the day initial treatment was administered was placed on the calf to maintain blinding of pen riders to treatment group; however, the pen riders may have been able to identify treatment group if the pen riders remembered when they pulled the calf the first time. Individual body weight and rectal temperature were collected for all cattle enrolled and recorded in a feedlot animal health computer system.[g] Cattle treated for BRD were returned to their home pen. Cattle were followed for 60 d to monitor subsequent health outcomes by feedlot personnel blinded to treatment group.

BRD Retreatments

Cattle were eligible for retreatment within the 60-d monitoring period post-enrollment if identified by pen riders as morbid for BRD, met or exceeded the PTI period, and had a rectal temperature ≥ 104.0°F (≥ 40°C) or lost body weight from first treatment. Cattle which required a second treatment for BRD were administered enrofloxacin[h] (4.50 mg/lb [9.92 mg/kg] BW SC; 4.5 mL/ 100 lb of BW). A 3-d PTI was used after the second treatment for BRD. Cattle which required a third treatment for BRD were administered florfenicol[i] (18.1 mg/lb [40 mg/kg] BW SC; 6 mL/100 lb BW). No calves were marketed until they cleared the longest antibiotic withdrawal period from time of administration.

Gross Necropsies

A gross necropsy was performed by a veterinarian or trained feedlot personnel on all enrolled animals which died during the study. A cause of death was determined for each case that died during the monitoring period based upon visual observations. No diagnostic samples were collected.

Feed, Housing, and Water

Cattle were fed diets formulated to meet or exceed National Research Council[14] maintenance requirements. Feed rations consisted of steam flaked corn, wet distillers' grains, ground alfalfa hay, supplement, and ground prairie hay. No feed-grade antimicrobials for control of BRD were fed to cattle throughout the trial. Cattle were housed in dirt floor pens consistent with commercial feedlot operations. Water was provided *ad libitum* through an automatic float-activated system.

Data Management

Data management steps were completed in a spreadsheet.[f] Binary variables were created for treatment successes and case fatality risk health outcomes. Treatment success was defined as not requiring additional treatment for BRD, cause of death not due to BRD, or not railed due to BRD during the 60-d monitoring period. Case fatality risk was defined as cattle dying due to BRD during the 60-d monitoring period. Treatment-death interval was calculated from day of first treatment for BRD to the day of death for cattle that died of BRD during the monitoring period. The BRD outs was calculated as died due to BRD or railed due to BRD. Dairy-beef and native beef cattle were categorized at the lot level.

Statistical Analyses

Data were imported into a commercial software package[j] for analyses. Data analyses were aligned with the randomized complete block design and animal as the experimental unit assigned to 1 of 4 PTI treatments within lots. General and generalized linear mixed models were used for statistical analyses with distributions and standard link functions aligned with the outcome variable: Gaussian, binomial, and cumulative logistic for continuous (days on feed, BW, and rectal temperature), dichotomous (heifer, dairy-beef, treatment success, case fatality risk, and mortality), and ordinal (clinical attitude score and metaphylaxis status) outcomes, respectively. Lot was included as a random intercept term in animal-level models. The PTI group and corresponding interaction terms were included in analyses of secondary objectives. Models were fitted with Kenward-Roger degrees of freedom approximation and Newton-Raphson and Ridging optimization procedures. An alpha=0.05 was used for all overall tests of treatment effects, and for subsequent pairwise comparisons an alpha=0.10 was used after adjusting for multiple comparisons using Tukey methods.

Results

A total of 800 cattle from 250 lots were enrolled in the study (Table 3). Cattle were enrolled from December 15, 2019 through April 20, 2020 with a range of body weight of 350 to 1348 lb (159 to 611 kg). There was no evidence that cattle characteristics differed among treatment groups at time of enrollment (Table 3; $P > 0.10$). First-treatment success ($P = 0.012$; Figure 1A), BRD case fatality risk ($P = 0.032$; Figure 1B), and BRD outs ($P = 0.039$) were all significantly associated with PTI (Table 4). The 3-d PTI treatment group had the lowest first-treatment success and was significantly ($P = 0.008$) different compared to the 9-d PTI treatment group which had the greatest first-treatment success. The 12-d PTI treatment group had the numerically poorest BRD case fatality risk and

Table 3. Characteristics of cattle at enrollment into treatment groups.* Model-adjusted means (SEM) from generalized linear mixed models with a random intercept to account for clustering within lots.

Parameter	3-day PTI	6-day PTI	9-day PTI	12-day PTI	Overall *P* value
No. cattle (No. lots)	196 (129)	187 (126)	208 (142)	209 (145)	-
Days on feed at enrollment, d	61.02 (3.43)	64.39 (3.46)	60.53 (3.39)	61.80 (3.38)	0.499
Body weight at enrollment, lb	818.49 (14.91)	848.06 (15.04)	830.45 (14.66)	831.77 (14.60)	0.165
Heifer, %	35.74 (6.35)	37.54 (6.50)	43.91 (6.48)	44.33 (6.40)	0.577
Dairy-beef, %	18.37 (2.77)	18.72 (2.85)	16.83 (2.59)	17.70 (2.64)	0.963
Rectal temperature, °F	104.93 (0.06)	104.92 (0.06)	104.88 (0.06)	104.87 (0.06)	0.893
Clinical attitude score, hd (%)					
1	91 (46.43)	92 (49.20)	110 (52.88)	96 (45.93)	0.310
2	95 (48.47)	86 (45.99)	93 (44.71)	102 (48.80)	
3	10 (5.10)	9 (4.81)	5 (2.40)	11 (5.26)	
Metaphylaxis, hd (%)					
None	151 (77.04)	143 (76.47)	157 (75.48)	154 (73.68)	0.968
Tilmicosin†	29 (14.80)	29 (15.51)	37 (17.79)	37 (17.70)	
Tulathromycin‡	16 (8.16)	15 (8.02)	14 (6.73)	18 (8.61)	

*Treatment groups: 3-, 6-, 9-, or 12-day post-treatment intervals (PTI) in feedlot cattle treated for BRD with gamithromycin
† Micotil®, Elanco Animal Health, Greenfield, IN
‡ Draxxin®, Zoetis Animal Health, Parsippany, NJ

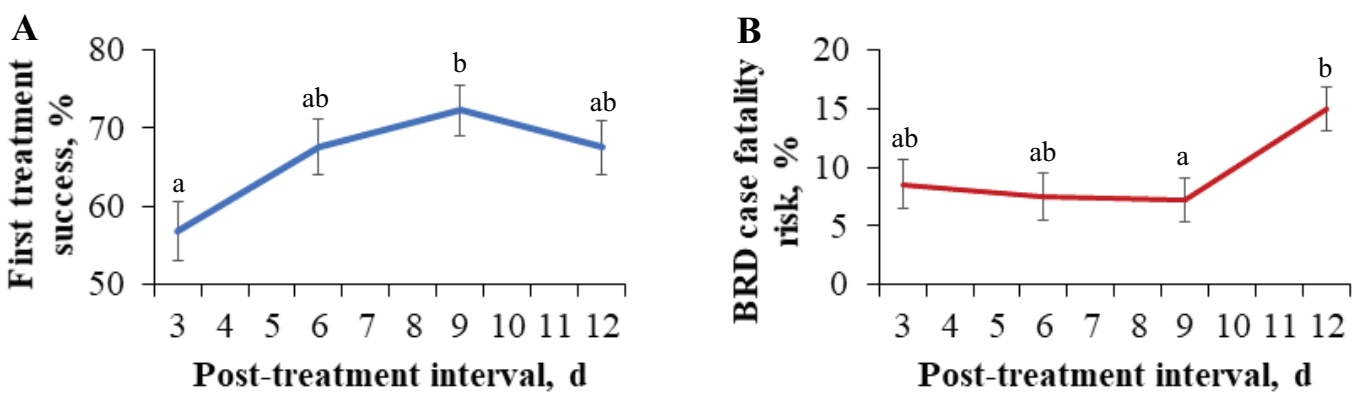

Figure 1. Outcome means (± SEM) first treatment success (A) and bovine respiratory disease (BRD) case fatality risk by post-treatment interval. Generalized linear mixed models included a random intercept to account for clustering within lots. Means without common superscripts differ (P <0.10; adjusted for multiple comparisons).

Table 4. Outcome means (± SEM) by treatment group* from generalized linear mixed models with a random intercept to account for clustering within lots. Means without common superscripts differ (*P* <0.10; adjusted for multiple comparisons).

Outcome	3-day PTI	6-day PTI	9-day PTI	12-day PTI	Overall *P* value
First treatment success,† %	56.83^{a} ± 3.75	67.60^{ab} ± 3.61	72.30^{b} ± 3.26	67.55^{ab} ± 3.41	0.012
Second treatment success,† %	61.01 ± 5.85	45.76 ± 7.03	56.06 ± 7.46	58.02 ± 7.30	0.397
Third treatment success,† %	71.02 ± 8.94	84.04 ± 7.73	80.39 ± 9.56	45.15 ± 13.86	0.099
Treatment death interval, d	19.27 ± 4.41	22.00 ± 4.66	21.02 ± 4.36	23.59 ± 3.26	0.879
BRD case fatality risk, %	8.56^{ab} ± 2.07	7.56^{ab} ± 2.01	7.24^{a} ± 1.86	15.02^{b} ± 2.64	0.032
Dead, %	9.06 ± 2.12	8.62 ± 2.12	8.72 ± 2.04	15.48 ± 2.66	0.076
BRD outs, %	8.59^{ab} ± 2.08	8.11^{ab} ± 2.09	7.26^{a} ± 1.87	15.07^{b} ± 2.64	0.039
Total outs, %	9.08 ± 2.13	9.18 ± 2.21	8.75 ± 2.04	15.52 ± 2.67	0.090

*Treatment groups: 3-, 6-, 9-, or 12-day post-treatment intervals (PTI) in feedlot cattle treated for BRD with gamithromycin
† Treatment success was defined as not requiring additional treatment for BRD, cause of death not due to BRD, or not railed due to BRD.

BRD outs; the BRD case fatality (P = 0.071) and BRD outs (P = 0.071) were both significantly different for 9-d PTI and 12-d PTI treatment group pairwise comparisons.

A total of 143 cattle (from 31 lots) were enrolled which were dairy-beef cross cattle and 657 (from 219 lots) were native cattle (Table 5). The dairy-beef cattle were enrolled at later DOF ($P = 0.012$) with lighter BW ($P < 0.001$) compared to the native cattle. The dairy-beef cattle also had decreased clinical attitude score ($P = 0.049$) and less use of metaphylaxis ($P < 0.001$) compared to native cattle at time of enrollment. There was no evidence for significant interactions between PTI treatment group and cattle type (Table 6); however, dairy-beef had decreased third treatment success ($P = 0.015$), greater BRD case fatality risk ($P = 0.012$), greater death loss ($P = 0.036$), greater BRD outs ($P = 0.016$), and greater total outs ($P = 0.043$) compared to the native cattle health outcomes (Table 6).

Discussion

To the authors' knowledge, this is the first study to look at different PTIs for gamithromycin in naturally occurring BRD cases. Results of the current study support extending the PTI up to 6- or 9-d after initial treatment with gamithromycin with no adverse animal health outcomes; however, extending the PTI to 12-d resulted in increased case fatality. These results help provide recommendations for judicious use of antimicrobials resulting in decreased selection for antimicrobial-resistant pathogens in the field.[3,6]

Previous studies, with different antimicrobials, have evaluated different PTIs with similar results to the current study.[20,21,22] Evaluation of health outcomes with only a 3-d PTI may result in an overestimation of treatment failures which agrees with other macrolide evaluations.[5] Allowing cattle to be treated with additional antimicrobials at the 3-d PTI

Table 5. Characteristics of native vs dairy type cattle at enrollment into a study comparing 4 post-treatment intervals (PTI) following treatment of BRD with gamithromycin. Model-adjusted means (SEM) unless otherwise noted.

Parameter	Dairy-beef	Native	Overall *P* value
No. cattle (No. lots)	143 (31)	657 (219)	-
Days-on-feed at enrollment, d	81.44 (8.28)	58.97 (3.17)	0.012
Body weight at enrollment, lb	619.45 (31.24)	861.64 (12.12)	<0.001
Heifer, %	25.73 (9.78)	43.27 (4.89)	0.152
Rectal temperature, °F	104.75 (0.04)	104.92(0.10)	0.101
Clinical attitude score, hd (%)			
1	85 (59.44)	304 (46.27)	0.049
2	54 (37.76)	322 (49.01)	
3	4 (2.80)	31 (4.72)	
Metaphylaxis, hd (%)			
None	133 (93.01)	472 (71.84)	<0.001
Tilmicosin*	0 (0.00)	132 (20.09)	
Tulathromycin†	10 (6.99)	53 (8.07)	

* Micotil®, Elanco Animal Health, Greenfield, IN

† Draxxin®, Zoetis Animal Health, Parsippany, NJ

Table 6. Outcome means (± SEM) by cattle type from generalized linear mixed models with a random intercept to account for clustering within lots in a study comparing 4 post-treatment intervals following treatment of BRD with gamithromycin.

Parameter	Dairy-beef			Native			Dairy-beef /native *P* value	PTI interaction *P* value*
First treatment success,* %	61.88	±	5.06	67.16	±	2.13	0.328	0.730
Second treatment success,* %	45.20	±	8.61	57.42	±	4.05	0.210	0.342
Third treatment success,* %	43.18	±	13.36	81.53	±	5.99	0.015	0.574
BRD case fatality risk, %	16.39	±	3.96	7.66	±	1.19	0.012	0.483
Dead, %	16.38	±	3.95	8.86	±	1.27	0.036	0.643
BRD outs, %	16.39	±	3.97	7.91	±	1.21	0.016	0.552
Total outs, %	16.39	±	3.96	9.10	±	1.29	0.043	0.705

* Treatment success was defined as not requiring additional treatment for BRD, cause of death due to BRD, or railed due to BRD.

resulted in no improvement in BRD case fatality or mortality outcomes. Extending the PTI to 6 or 9 d, allowed additional time for the cattle to return to normal based on visual appearance or provided additional time for the exposure of the drug concentration to improve health outcomes as previously suggested;[3] however, extending the PTI to 12 d resulted in sub-optimal health outcomes. Gamithromycin has been detected 10 d after initial treatment for BRD in the plasma and pulmonary epithelial lining fluid, but the researchers did not evaluate concentrations in plasma or pulmonary epithelial lining fluid after 10 d.[7] The current study had optimal health outcomes at the 6-d and 9-d PTI treatment groups. Pharmacodynamics and pharmacokinetic data have at times provided misleading optimal PTI recommendations;[3] however, results from the current study agree with the pharmacokinetic data of gamithromycin being present in the plasma and pulmonary epithelial lining fluid for up to 10 d.[7] The authors recommend performing clinical field studies to determine optimal PTI recommendations. Determination of the PTI used in the field needs to optimize the animal health outcomes as well as include labor, treatment costs, and the ability of the feedlot crew to withhold treatment of cattle based on poor appearance in the midpoint of the PTI.

Previous studies have compared the efficacy of gamithromycin to other antimicrobials for initial BRD treatment[28,31] and metaphylaxis.[2,23,29,32] Van Donkersgoed et al used a 5-d PTI following initial treatment for BRD compared to florfenicol, and identified no health outcome differences between the 2 treatment groups.[31] Torres et al identified a higher retreatment risk in cattle administered gamithromycin compared to cattle administered tulathromycin; however, the PTI used for the gamithromycin or tulathromycin treatments groups was not stated.[28] Meta-analyses also have been performed for summarizing the outcomes for BRD treatment[18,16] and metaphylaxis;[1,15,17] however, none of the meta-analyses have accounted for PTI or post-metaphylaxis intervals used which may impact health outcomes. Consideration of the PTI used, study population, and referent population is needed to make appropriate comparisons between antimicrobials as previously described.[26]

Health outcomes of the dairy-beef cattle provide some novel results as the dairy-beef population is becoming more frequent in the feedlot industry.[30] There were no interactions between metaphylaxis status and cattle type, indicating same PTIs can be used in the dairy-beef cattle type as native cattle. Overall treatment response was poorer in the dairy-beef cattle compared to the native cattle. It is important to note the dairy-beef cattle had a lower average BW compared to the native cattle, and BW has been previously associated with treatment response.[4,27] The authors hypothesize if BW was similar between the dairy-beef and native cattle, health outcomes may have been similar as well; however, additional research is needed to support or refute this hypothesis.

A limitation of the current study was monitoring for 60 d post-enrollment, and no performance outcomes were collected; however, the primary objective of the study was to evaluate health outcomes. The 60-d monitoring period is beyond the 35-d monitoring period previously suggested.[28] Capturing data on performance outcomes may have put increased strain on the hospital management system and resulted in decreased health outcomes, which then may not represent outcomes observed in the field.[9,33] Another potential limitation of the study was the possibility of the pen rider to become unblinded to treatment group if the pen rider remembered when an individual calf was pulled to detect PTI treatment group; however, each pen rider was evaluating approximately 8,000 calves each day. Each lot could have new animals enrolled into the study each day resulting in different eligible retreatment dates, making it difficult to identify the PTI treatment group allocation. The study was not initially designed or powered to identify a difference in health outcomes by cattle type; however, these results provide initial results for future studies.

Conclusions

Optimal PTI for gamithromycin was 6 d or 9 d based on health outcomes. A 3-d PTI following initial treatment with gamithromycin resulted in decreased first-treatment success. The 12-d PTI treatment group resulted in increased BRD case fatality risk. There were no significant differences in health outcomes between the 6- and the 9-d PTI groups. There were no interactions between cattle type indicating the same PTIs can be used in the dairy-beef cattle type as native cattle; however, overall treatment response was poor in the dairy-beef cattle compared to the native cattle. Determination of the PTI used in the field needs to optimize the animal health outcomes as well as include the labor, treatment costs, and ability of the feedlot crew to withhold treatment of cattle based on poor appearance in the midpoint of the PTI. The results of the study will help practitioners to optimally use gamithromycin antimicrobial related to animal health outcomes.

Endnotes

[a] Zactran®, Boehringer Ingelheim Animal Health USA, Inc., Duluth, GA
[b] Micotil®, Elanco Animal Health, Greenfield, IN
[c] Draxxin®, Zoetis Animal Health, Parsippany, NJ
[d] Excede®, Zoetis Animal Health, Parsippany, NJ
[e] R Studio Team 2016, Boston, MA
[f] Microsoft Office Excel, Microsoft Corp, Redman, WA
[g] Animal Management System, Animal Health International, Greeley, CO
[h] Baytril®, Bayer Animal Health, Shawnee, KS
[i] Nuflor®, Merck Animal Health, Whitehouse Station, NJ
[j] SAS Glimmix, Version 9.4, SAS Institute Inc, Cary, NC

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References

1. Abell KM, Theurer ME, Larson RL, White BJ, Apley M. A mixed treatment comparison meta-analysis of metaphylaxis treatments for bovine respiratory disease in beef cattle. *J Anim Sci* 2017; 95:626–635.
2. Amrine D, White B, Goehl D, Sweiger SH, Nosky B, Tessman RK. Comparisons of metaphylactic treatments of Zactran® (gamithromycin) vs Excede® (ceftiofur crystalline free acid) in high risk, stocker calves. *Intern J Appl Res Vet Med* 2014; 12:221–228.
3. Apley MD. Treatment of calves with bovine respiratory disease: Duration of therapy and posttreatment intervals. *Vet Clin North Am Food Anim Pract* 2015; 31:441–453.
4. Avra TD, Abell KM, Shane DD, Theurer ME, Larson RL, White BJ. A retrospective analysis of risk factors associated with bovine respiratory disease treatment failure in feedlot cattle. *J Anim Sci* 2017; 95:1521–1527.
5. Carter BL, McClary D, Mechor GD, Christmas RA, Corbin MJ, Guthrie CA. Comparison of 3-, 5-, and 7-day post-treatment evaluation periods for measuring therapeutic response to tilmicosin treatment of bovine respiratory disease. *Bov Pract* 2006; 40:97–101.
6. DeDonder KD, Apley MD. A review of the expected effects of antimicrobials in bovine respiratory disease treatment and control using outcomes from published randomized clinical trials with negative controls. *Vet Clin North Am Food Anim Pract* 2015; 31:97–111.
7. DeDonder KD, Apley MD, Li M, Gehring R, Harhay DM, Lubbers BV, White BJ, Capik SF, KuKanich B, Riviere JE, Tessman RK. Pharmacokinetics and pharmacodynamics of gamithromycin in pulmonary epithelial lining fluid in naturally occurring bovine respiratory disease in multisource commingled feedlot cattle. *J Vet Pharmacol Ther* 2016; 39:157–166.
8. Forbes AB, Ramage C, Sales J, Baggott D, Donachie W. 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.
9. Fox JT. Management of feedyard hospitals. *Vet Clin North Am Food Anim Pract* 2015; 31:455–463.
10. Giguère S, Huang R, Malinski TJ, Dorr PM, Tessman RK, Somerville BA. Disposition of gamithromycin in plasma, pulmonary epithelial lining fluid, bronchoalveolar cells, and lung tissue in cattle. *Am J Vet Res* 2011; 72:326–330.
11. Huang RA, Letendre LT, Banav N, Fischer J, Somerville B. Pharmacokinetics of gamithromycin in cattle with comparison of plasma and lung tissue concentrations and plasma antibacterial activity. *J Vet Pharmacol Ther* 2010; 33:227–237.
12. Jain R, Danziger LH. The macrolide antibiotics: a pharmacokinetic and pharmacodynamic overview. *Curr Pharm Des* 2004; 10:3045–3053.
13. Lechtenberg KF, Daniels CS, Schieber T, Bechtol DT, Drag M, Kunkle BN, Chester ST, Tessman RK. Field efficacy study of gamithromycin for the treatment of bovine respiratory disease associated with *Mycoplasma bovis* in beef and non-lactating dairy cattle. *Intern J Appl Res Vet Med* 2011; 9:225–232.
14. National Research Council. *Nutrient requirements of beef cattle*. 8th ed. Washington DC: Natl Acad Press, 2016.
15. Nautrup BP, Ilse Van Vlaenderen D, Decker M, Cleale RM. Antimicrobial drug use for control and treatment of bovine respiratory disease in US feedlot cattle: A meta-analysis of comparative studies versus tulathromycin. *Bov Pract* 2017; 51:1–13.
16. O'Connor AM, Coetzee JF, da Silva N, Wang C. A mixed treatment comparison meta-analysis of antibiotic treatments for bovine respiratory disease. *Prev Vet Med* 2013; 110:77–87.
17. O'Connor AM, Hu D, Totton SC, Scott N, Winder CB, Wang B, Wang C, Glanville J, Wood H, White B, Larson R, Waldner C, Sargeant JM. A systematic review and network meta-analysis of injectable antibiotic options for the control of bovine respiratory disease in the first 45 days post arrival at the feedlot. *Anim Health Res Rev* 2019; 20:163–181.
18. O'Connor AM, Yuan C, Cullen JN, Coetzee JF, da Silva N, Wang C. A mixed treatment meta-analysis of antibiotic treatment options for bovine respiratory disease - An update. *Prev Vet Med* 2016; 132:130–139.
19. O'Ferrall G, Ryan M. Beef crossing: Effects of genotype of the foetus on the performance of dairy cows. *Irish J Agric Res* 1990; 29:101–108.
20. Pfizer. Efficacy of Draxxin®, followed by 7-, 10-, or 14-day post-treatment intervals, against naturally occurring bovine respiratory disease. Prepared from study report 1133R-60-05-489; 2006.
21. Pfizer. Efficacy of Excede followed by 3- or 7- day post-treatment intervals vs Baytril followed by a 3-day post-treatment interval in treatment of bovine respiratory disease. Technical Bulletin No. EXD04024; 2004.
22. Pfizer. Outcomes of 3–, 5-, or 7-day post-treatment intervals after a single administration of Excede. Technical Bulletin No. EXD04023; 2004.
23. Rossi S, Vandoni SL, Bonfanti M, Forbes AB. Effects of arrival medication with gamithromycin on bovine respiratory disease in feedlot cattle in Italy. *Intern J Appl Res Vet Med* 2010; 8:87–96.
24. Scanavez A, Mendonça L. Gestation length and overall performance in the subsequent lactation of dairy cows conceiving to Holstein, Jersey, or Angus semen: An observational study. Kansas Agric Exp Stn Res Reports; 2018. Available at: https://newprairiepress.org/kaesrr/vol4/iss10/7.
25. Sifferman RL, Wolff WA, Holste JE, Smith LL, Drag MD, Yoon S, Kunkle BN, Tessman RK. Field efficacy evaluation of gamithromycin for treatment of bovine respiratory disease in cattle at feedlots. *Intern J Appl Res Vet Med* 2011; 9:166–175.
26. Theurer ME, Fox JT, Bryant LK, Nickell JS, Hutcheson JP. Treatment efficacy of tildipirosin or tulathromycin for first treatment of naturally occurring bovine respiratory disease in a commercial feedlot. *Bov Pract* 2018; 52:154–159.
27. Theurer ME, White BJ, Larson RL, Holstein KK, Amrine DE. Relationship between rectal temperature at first treatment for bovine respiratory disease complex in feedlot calves and the probability of not finishing the production cycle. *J Am Vet Med Assoc* 2014; 245:1279–1285.
28. Torres S, Thomson DU, Bello NM, Nosky BJ, Reinhardt CD. Field study of the comparative efficacy of gamithromycin and tulathromycin for the treatment of undifferentiated bovine respiratory disease complex in beef feedlot calves. *Am J Vet Res* 2013; 74:847–853.
29. Torres S, Thomson DU, Bello NM, Nosky BJ, Reinhardt CD. 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.
30. USDA. Dairy cattle management practices in the United States, 2014. In: APHIS, ed. Fort Collins, CO: National Animal Health Monitoring System. 2016;1-246.
31. Van Donkersgoed J, Hendrick S. Clinical efficacy of gamithromycin versus florfenicol for the treatment of undifferentiated fever in winter-placed feedlot calves. *Bov Pract* 2013; 47:152–156.
32. Van Donkersgoed J, Merrill JK. A comparison of tilmicosin to gamithromycin for on arrival treatment of bovine respiratory disease in feeder steers. *Bov Pract* 2012; 46:46–51.
33. White BJ, Larson RL, Theurer ME. Interpreting statistics from published research to answer clinical and management questions. *J Anim Sci* 2016; 94:4959–4971.

